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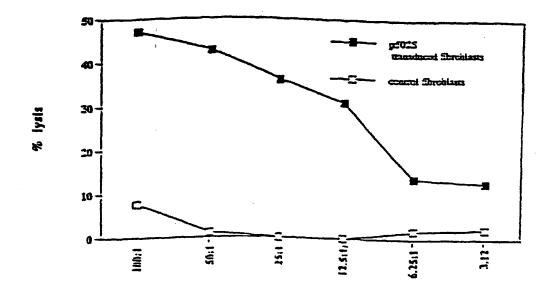
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[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER



Effector: Target Ratio

(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, particularly prostate cancer, are disclosed. Illustrative compositions comprise one or more prostate-specific polypeptides, immunogenic portions thereof, polynucleotides that encode such polypeptides, antigen presenting cell that expresses such polypeptides, and T cells that are specific for cells expressing such polypeptides. The disclosed compositions are useful, for example, in the diagnosis, prevention and/or treatment of diseases, particularly prostate cancer.



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## COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER

### TECHNICAL FIELD OF THE INVENTION

The present invention relates generally to therapy and diagnosis of cancer, such as prostate cancer. The invention is more specifically related to polypeptides, comprising at least a portion of a prostate-specific protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides are useful in pharmaceutical compositions, e.g., vaccines, and other compositions for the diagnosis and treatment of prostate cancer.

#### BACKGROUND OF THE INVENTION

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Cancer is a significant health problem throughout the world. Although Cancer is a significant health problem throughout the world. Although advances have been made in detection and therapy of cancer, no vaccine or other universally successful method for prevention or treatment is currently available. Current therapies, which are generally based on a combination of chemotherapy or surgery and radiation, continue to prove inadequate in many patients.

Prostate cancer is the most common form of cancer among males, with an estimated incidence of 30% in men over the age of 50. Overwhelming clinical evidence shows that human prostate cancer has the propensity to metastasize to bone, and the disease appears to progress inevitably from androgen dependent to androgen refractory status, leading to increased patient mortality. This prevalent disease is currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate cancer remains difficult to treat. Commonly, treatment is based on surgery and/or radiation therapy, but these methods are ineffective in a significant percentage of cases. Two previously identified prostate specific proteins - prostate specific antigen (PSA)

and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic potential. For example, PSA levels do not always correlate well with the presence of prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

### 10 SUMMARY OF THE INVENTION

In one aspect, the present invention provides polynucleotide compositions comprising a sequence selected from the group consisting of:

- (a) sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 and 786-788;
- (b) complements of the sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 and 786-788;
  - (c) sequences consisting of at least 20 contiguous residues of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 and 786-788;
  - (d) sequences that hybridize to a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375,

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381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 and 786-788, under moderately stringent conditions;

- 5 (e) sequences having at least 75% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 and 786-788;
- 10 (f) sequences having at least 90% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 and 786-788; and
  - 15 (g) degenerate variants of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 and 786-788.
- In one preferred embodiment, the polynucleotide compositions of the invention are expressed in at least about 20%, more preferably in at least about 30%, and most preferably in at least about 50% of prostate tissue samples tested, at a level that is at least about 2-fold, preferably at least about 5-fold, and most preferably at least about 10-fold higher than that for other normal tissues.
- The present invention, in another aspect, provides polypeptide compositions comprising an amino acid sequence that is encoded by a polynucleotide sequence described above.

The present invention further provides polypeptide compositions comprising an amino acid sequence selected from the group consisting of sequences recited in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383,

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477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 627-629, 632, 633, 635, 637, 638, 656-671, 675, 683, 684, 710, 712, 714, 715, 717-719, 723-734, 736, 740-750, 752, 754, 755, 766-772, 777-785 and 789-791.

In certain preferred embodiments, the polypeptides and/or polynucleotides of the present invention are immunogenic, *i.e.*, they are capable of eliciting an immune response, particularly a humoral and/or cellular immune response, as further described herein.

The present invention further provides fragments, variants and/or derivatives of the disclosed polypeptide and/or polynucleotide sequences, wherein the fragments, variants and/or derivatives preferably have a level of immunogenic activity of at least about 50%, preferably at least about 70% and more preferably at least about 90% of the level of immunogenic activity of a polypeptide sequence set forth in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 627-629, 632, 633, 635, 637, 638, 656-671, 675, 683, 684, 710, 712, 714, 715, 717-719, 723-734, 736, 740-750, 752, 754, 755, 766-772, 777-785 or 789-791, or a polypeptide sequence encoded by a polynucleotide sequence set forth in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 and 786-788.

The present invention further provides polynucleotides that encode a polypeptide described above, expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, pharmaceutical compositions, e.g., vaccine compositions, are provided for prophylactic or therapeutic applications. Such compositions generally comprise an immunogenic polypeptide or

polynucleotide of the invention and an immunostimulant, such as an adjuvant, together with a physiologically acceptable carrier.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to 5 a polypeptide of the present invention, or a fragment thereof; and (b) a physiologically acceptable carrier.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Illustrative 10 antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts

Within related aspects, pharmaceutical compositions are provided that and B cells. comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins, typically in the form of pharmaceutical compositions, e.g., vaccine compositions, comprising a physiologically acceptable carrier and/or an immunostimulant. The fusions proteins may comprise multiple immunogenic 20 polypeptides or portions/variants thereof, as described herein, and may further comprise one or more polypeptide segments for facilitating and/or enhancing the expression, purification and/or immunogenicity of the polypeptide(s).

Within further aspects, the present invention provides methods for stimulating an immune response in a patient, preferably a T cell response in a human 25 patient, comprising administering a pharmaceutical composition described herein. The patient may be afflicted with prostate cancer, in which case the methods provide treatment for the disease, or a patient considered to be at risk for such a disease may be treated prophylactically.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a 30

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patient a pharmaceutical composition as recited above. The patient may be afflicted with prostate cancer, in which case the methods provide treatment for the disease, or a patient considered to be at risk for such a disease may be treated prophylactically.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a polypeptide of the present invention, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the polypeptide from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

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Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a polypeptide of the present invention, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of polypeptide disclosed herein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

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Within further aspects, the present invention provides methods for determining the presence or absence of a cancer, preferably a prostate cancer, in a patient comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b), and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide of the present invention; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide of the present invention, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to an inventive polynucleotide, or a complement of such a polynucleotide.

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In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide of the present invention; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b), and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

### BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate-specific polypeptide P502S, as compared to control fibroblasts. The percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells expressing the representative prostate-specific polypeptide P502S. In each case, the number of  $\gamma$ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/neu.

Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release

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bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.

Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse Jurkat A2Kb cells expressing the representative prostate-specific polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

Figures 6A and 6B are graphs illustrating the specificity of a CD8<sup>+</sup> cell line (3A-1) for a representative prostate-specific antigen (P501S). Figure 6A shows the results of a <sup>51</sup>Cr release assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferongamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target rations as indicated.

Figure 7 is a Western blot showing the expression of P501S in baculovirus.

Figure 8 illustrates the results of epitope mapping studies on P501S.

Figure 9 is a schematic representation of the P501S protein showing the location of transmembrane domains and predicted intracellular and extracellular domains.

Figure 10 is a genomic map showing the location of the prostate genes P775P, P704P, B305D, P712P and P774P within the Cat Eye Syndrome region of chromosome 22q11.2

Figure 11 shows the results of an ELISA assay to determine the specificity of rabbit polyclonal antisera raised against P501S.

SEQ ID NO: 1 is the determined cDNA sequence for F1-13 SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12

SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12

•	SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16
	SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1
	SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9
	SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4
5	SEQ ID NO: 8 is the determined 3' cDNA sequence for J1-17
	SEQ ID NO: 9 is the determined 5' cDNA sequence for J1-17
	SEQ ID NO: 10 is the determined 3' cDNA sequence for L1-12
•	SEQ ID NO: 11 is the determined 5' cDNA sequence for L1-12
	SEQ ID NO: 12 is the determined 3' cDNA sequence for N1-1862
10	SEQ ID NO: 13 is the determined 5' cDNA sequence for N1-1862
1	SEQ ID NO: 14 is the determined 3' cDNA sequence for J1-13
	SEQ ID NO: 15 is the determined 5' cDNA sequence for J1-13
	SEQ ID NO: 16 is the determined 3' cDNA sequence for J1-19
•	SEQ ID NO: 17 is the determined 5' cDNA sequence for J1-19
15	SEQ ID NO: 18 is the determined 3' cDNA sequence for J1-25
	SEQ ID NO: 19 is the determined 5' cDNA sequence for J1-25
	SEQ ID NO: 20 is the determined 5' cDNA sequence for J1-24
	SEQ ID NO: 21 is the determined 3' cDNA sequence for J1-24
	SEQ ID NO: 22 is the determined 5' cDNA sequence for K1-58
20	SEQ ID NO: 23 is the determined 3' cDNA sequence for K1-58
	SEQ ID NO: 24 is the determined 5' cDNA sequence for K1-63
	SEQ ID NO: 25 is the determined 3' cDNA sequence for K1-63
	SEQ ID NO: 26 is the determined 5' cDNA sequence for L1-4
	SEQ ID NO: 27 is the determined 3' cDNA sequence for L1-4
25	SEQ ID NO: 28 is the determined 5' cDNA sequence for L1-14
	SEQ ID NO: 29 is the determined 3' cDNA sequence for L1-14
	SEQ ID NO: 30 is the determined 3' cDNA sequence for J1-12
	SEQ ID NO: 31 is the determined 3' cDNA sequence for J1-16
	SEQ ID NO: 32 is the determined 3' cDNA sequence for J1-21
30	SEQ ID NO: 33 is the determined 3' cDNA sequence for K1-48

	SEQ ID NO: 34 is the determined 3' cDNA sequence for K1-55
	SEQ ID NO: 35 is the determined 3' cDNA sequence for L1-2
	SEQ ID NO: 36 is the determined 3' cDNA sequence for L1-6
	SEQ ID NO: 37 is the determined 3' cDNA sequence for N1-1858
5	SEQ ID NO: 38 is the determined 3' cDNA sequence for N1-1860
	SEQ ID NO: 39 is the determined 3' cDNA sequence for N1-1861
	SEQ ID NO: 40 is the determined 3' cDNA sequence for N1-1864
	SEQ ID NO: 41 is the determined cDNA sequence for P5
	SEQ ID NO: 42 is the determined cDNA sequence for P8
10	SEQ ID NO: 43 is the determined cDNA sequence for P9
	SEQ ID NO: 44 is the determined cDNA sequence for P18
	SEQ ID NO: 45 is the determined cDNA sequence for P20
	SEQ ID NO: 46 is the determined cDNA sequence for P29
	SEQ ID NO: 47 is the determined cDNA sequence for P30
15	SEQ ID NO: 48 is the determined cDNA sequence for P34
	SEQ ID NO: 49 is the determined cDNA sequence for P36
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	SEQ ID NO: 51 is the determined cDNA sequence for P39
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	SEQ ID NO: 55 is the determined cDNA sequence for P50
	SEQ ID NO: 56 is the determined cDNA sequence for P53
	SEQ ID NO: 57 is the determined cDNA sequence for P55
25	SEQ ID NO: 58 is the determined cDNA sequence for P60
ye <sup>n</sup> es .	SEQ ID NO: 59 is the determined cDNA sequence for P64
	SEQ ID NO: 60 is the determined cDNA sequence for P65
	SEQ ID NO: 61 is the determined cDNA sequence for P73
	SEQ ID NO: 62 is the determined cDNA sequence for P75
30	SEQ ID NO: 63 is the determined cDNA sequence for P76

SEQ ID NO: 64 is the determined cDNA sequence for P79 SEQ ID NO: 65 is the determined cDNA sequence for P84 SEQ ID NO: 66 is the determined cDNA sequence for P68 SEQ ID NO: 67 is the determined cDNA sequence for P80 (also referred SEQ ID NO: 68 is the determined cDNA sequence for P82

SEQ ID NO: 69 is the determined cDNA sequence for U1-3064

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to as P704P)

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SEQ ID NO: 70 is the determined cDNA sequence for U1-3065 SEQ ID NO: 71 is the determined cDNA sequence for V1-3692 SEQ ID NO: 72 is the determined cDNA sequence for 1A-3905 SEQ ID NO: 73 is the determined cDNA sequence for V1-3686 SEQ ID NO: 74 is the determined cDNA sequence for R1-2330 SEQ ID NO: 75 is the determined cDNA sequence for 1B-3976 SEQ ID NO: 76 is the determined cDNA sequence for V1-3679 SEQ ID NO: 77 is the determined cDNA sequence for 1G-4736 SEO ID NO: 78 is the determined cDNA sequence for 1G-4738 SEQ ID NO: 79 is the determined cDNA sequence for 1G-4741 SEQ ID NO: 80 is the determined cDNA sequence for 1G-4744 SEQ ID NO: 81 is the determined cDNA sequence for 1G-4734 SEQ ID NO: 82 is the determined cDNA sequence for 1H-4774 SEQ ID NO: 83 is the determined cDNA sequence for 1H-4781 SEQ ID NO: 84 is the determined cDNA sequence for 1H-4785 SEQ ID NO: 85 is the determined cDNA sequence for 1H-4787 SEQ ID NO: 86 is the determined cDNA sequence for 1H-4796 SEQ ID NO: 87 is the determined cDNA sequence for 11-4807 SEQ ID NO: 88 is the determined cDNA sequence for 1I-4810 SEQ ID NO: 89 is the determined cDNA sequence for 1I-4811 SEQ ID NO: 90 is the determined cDNA sequence for 1J-4876 SEQ ID NO: 91 is the determined cDNA sequence for 1K-4884

SEQ ID NO: 92 is the determined cDNA sequence for 1K-4896

ı		SEQ ID NO: 93 is the determined cDNA sequence for 1G-4761
		SEQ ID NO: 94 is the determined cDNA sequence for 1G-4762
		SEQ ID NO: 95 is the determined cDNA sequence for 1H-4766
: _		SEQ ID NO: 96 is the determined cDNA sequence for 1H-4770
. 5		SEQ ID NO: 97 is the determined cDNA sequence for 1H-4771
		SEQ ID NO: 98 is the determined cDNA sequence for 1H-4772
		SEQ ID NO: 99 is the determined cDNA sequence for 1D-4297
	•	SEQ ID NO: 100 is the determined cDNA sequence for 1D-4309
·		SEQ ID NO: 101 is the determined cDNA sequence for 1D.1-4278
10		SEQ ID NO: 102 is the determined cDNA sequence for 1D-4288
		SEQ ID NO: 103 is the determined cDNA sequence for 1D-4283
,		SEQ ID NO: 104 is the determined cDNA sequence for 1D-4304
	1	SEQ ID NO: 105 is the determined cDNA sequence for 1D-4296
		SEQ ID NO: 106 is the determined cDNA sequence for 1D-4280
15		SEQ ID NO: 107 is the determined full length cDNA sequence for F1-12
	(also referred	to as P504S)
		SEQ ID NO: 108 is the predicted amino acid sequence for F1-12
		SEQ ID NO: 109 is the determined full length cDNA sequence for J1-17
		SEQ ID NO: 110 is the determined full length cDNA sequence for L1-12
20	(also referred	to as P501S)
<		SEQ ID NO: 111 is the determined full length cDNA sequence for N1
	1862 (also ref	Cerred to as P503S)
	14.5 TV 14 15	SEQ ID NO: 112 is the predicted amino acid sequence for J1-17
	被持有。	SEQ ID NO: 113 is the predicted amino acid sequence for L1-12 (also
25	referred to as	P501S)
•	1 14. Ec 1.	SEQ ID NO: 114 is the predicted amino acid sequence for N1-1862 (also
	referred to as	P503S)
		SEQ ID NO: 115 is the determined cDNA sequence for P89
	e <sup>-</sup>	SEQ ID NO: 116 is the determined cDNA sequence for P90
30	•	SEQ ID NO: 117 is the determined cDNA sequence for P92

	SEQ ID NO: 118 is the determined cDNA sequence for P95
	SEQ ID NO: 119 is the determined cDNA sequence for P98
	SEQ ID NO: 120 is the determined cDNA sequence for P102
	SEQ ID NO: 121 is the determined cDNA sequence for P110
5	SEQ ID NO: 122 is the determined cDNA sequence for P111
	SEQ ID NO: 123 is the determined cDNA sequence for P114
	SEQ ID NO: 124 is the determined cDNA sequence for P115
-	SEQ ID NO: 125 is the determined cDNA sequence for P116
	SEQ ID NO: 126 is the determined cDNA sequence for P124
10	SEQ ID NO: 127 is the determined cDNA sequence for P126
	SEQ ID NO: 128 is the determined cDNA sequence for P130
	SEQ ID NO: 129 is the determined cDNA sequence for P133
	SEQ ID NO: 130 is the determined cDNA sequence for P138
	SEQ ID NO: 131 is the determined cDNA sequence for P143
15	SEQ ID NO: 132 is the determined cDNA sequence for P151
	SEQ ID NO: 133 is the determined cDNA sequence for P156
	SEQ ID NO: 134 is the determined cDNA sequence for P157
	SEQ ID NO: 135 is the determined cDNA sequence for P166
	SEQ ID NO: 136 is the determined cDNA sequence for P176
20	SEQ ID NO: 137 is the determined cDNA sequence for P178
	SEQ ID NO: 138 is the determined cDNA sequence for P179
	SEQ ID NO: 139 is the determined cDNA sequence for P185
	SEQ ID NO: 140 is the determined cDNA sequence for P192
•	SEQ ID NO: 141 is the determined cDNA sequence for P201
25	SEQ ID NO: 142 is the determined cDNA sequence for P204
	SEQ ID NO: 143 is the determined cDNA sequence for P208
	SEQ ID NO: 144 is the determined cDNA sequence for P211
	SEQ ID NO: 145 is the determined cDNA sequence for P213
	SEQ ID NO: 146 is the determined cDNA sequence for P219
30	SEQ ID NO: 147 is the determined cDNA sequence for P237

	* ++	SEQ ID NO: 148 is the determined cDNA sequence for P239
		SEQ ID NO: 149 is the determined cDNA sequence for P248
~.	•	SEQ ID NO: 150 is the determined cDNA sequence for P251
1		SEQ ID NO: 151 is the determined cDNA sequence for P255
5		SEQ ID NO: 152 is the determined cDNA sequence for P256
	, 1	SEQ ID NO: 153 is the determined cDNA sequence for P259
		SEQ ID NO: 154 is the determined cDNA sequence for P260
****	•	SEQ ID NO: 155 is the determined cDNA sequence for P263
To p		SEQ ID NO: 156 is the determined cDNA sequence for P264
10		SEQ ID NO: 157 is the determined cDNA sequence for P266
		SEQ ID NO: 158 is the determined cDNA sequence for P270
		SEQ ID NO: 159 is the determined cDNA sequence for P272
		SEQ ID NO: 160 is the determined cDNA sequence for P278
•	٠.,	SEQ ID NO: 161 is the determined cDNA sequence for P105
15	•	SEQ ID NO: 162 is the determined cDNA sequence for P107
		SEQ ID NO: 163 is the determined cDNA sequence for P137
		SEQ ID NO: 164 is the determined cDNA sequence for P194
		SEQ ID NO: 165 is the determined cDNA sequence for P195
		SEQ ID NO: 166 is the determined cDNA sequence for P196
20	1.50	SEQ ID NO: 167 is the determined cDNA sequence for P220
		SEQ ID NO: 168 is the determined cDNA sequence for P234
		SEQ ID NO: 169 is the determined cDNA sequence for P235
	5	SEQ ID NO: 170 is the determined cDNA sequence for P243
4.1	193 0	SEQ ID NO: 171 is the determined cDNA sequence for P703P-DE1
25	33 75	SEQ ID NO: 172 is the predicted amino acid sequence for P703P-DE1
o inte		SEQ ID NO: 173 is the determined cDNA sequence for P703P-DE2
		SEQ ID NO: 174 is the determined cDNA sequence for P703P-DE6
	and the state of	SEQ ID NO: 175 is the determined cDNA sequence for P703P-DE13
		SEQ ID NO: 176 is the predicted amino acid sequence for P703P-DE13
30		SEQ ID NO: 177 is the determined cDNA sequence for P703P-DE14

		SEQ ID NO: 178 is the predicted amino acid sequence for P703P-DE14
		SEQ ID NO: 179 is the determined extended cDNA sequence for 1G-
	4736	
		SEQ ID NO: 180 is the determined extended cDNA sequence for 1G-
5	4738	
		SEQ ID NO: 181 is the determined extended cDNA sequence for 1G-
	4741	
	•	SEQ ID NO: 182 is the determined extended cDNA sequence for 1G-
	4744	
10		SEQ ID NO: 183 is the determined extended cDNA sequence for 1H-
	4774	
		SEQ ID NO: 184 is the determined extended cDNA sequence for 1H-
	4781	
*		SEQ ID NO: 185 is the determined extended cDNA sequence for 1H-
15	4785	
	4000	SEQ ID NO: 186 is the determined extended cDNA sequence for 1H-
	4787	
	4706	SEQ ID NO: 187 is the determined extended cDNA sequence for 1H-
20	4796	SEO ID NO. 100 is the determined and deliberation of the
20	4007	SEQ ID NO: 188 is the determined extended cDNA sequence for 1I-
	4807	SEO ID NO. 190 is the determined 2' aDNIA seguence for 11 4910
		SEQ ID NO: 189 is the determined 3' cDNA sequence for 1I-4810
		SEQ ID NO: 190 is the determined 3' cDNA sequence for 1I-4811 SEQ ID NO: 191 is the determined extended cDNA sequence for 1J-
25	4876	SEQ ID 140. 191 is the determined extended cDNA sequence for 13-
<b>2</b> .)	4070	SEO ID NO: 102 is the determined extended aDNA seguence for 1K
	4884	SEQ ID NO: 192 is the determined extended cDNA sequence for 1K-
	700 <del>7</del>	SEQ ID NO: 193 is the determined extended cDNA sequence for 1K-
	4896	550 to 110. 133 is the determined extended conta sequence for 1K-
	7070	

1		SEQ ID NO: 194 is the determined extended cDNA sequence for 1G-
	4761	
		SEQ ID NO: 195 is the determined extended cDNA sequence for 1G-
	4762	
5	• •	SEQ ID NO: 196 is the determined extended cDNA sequence for 1H-
	4766	
		SEQ ID NO: 197 is the determined 3' cDNA sequence for 1H-4770
	•	SEQ ID NO: 198 is the determined 3' cDNA sequence for 1H-4771
		SEQ ID NO: 199 is the determined extended cDNA sequence for 1H-
10	4772	
		SEQ ID NO: 200 is the determined extended cDNA sequence for 1D-
	4309	
	:	SEQ ID NO: 201 is the determined extended cDNA sequence for 1D.1-
	4278	
15		SEQ ID NO: 202 is the determined extended cDNA sequence for 1D-
	4288	
		SEQ ID NO: 203 is the determined extended cDNA sequence for 1D-
	4283	
		SEQ ID NO: 204 is the determined extended cDNA sequence for 1D-
20	4304	
		SEQ ID NO: 205 is the determined extended cDNA sequence for 1D-
	4296	
		SEQ ID NO: 206 is the determined extended cDNA sequence for 1D-
	4280	
25		SEQ ID NO: 207 is the determined cDNA sequence for 10-d8fwd
		SEQ ID NO: 208 is the determined cDNA sequence for 10-H10con
	• • • •	SEQ ID NO: 209 is the determined cDNA sequence for 11-C8rev
		SEQ ID NO: 210 is the determined cDNA sequence for 7.g6fwd
		SEQ ID NO: 211 is the determined cDNA sequence for 7.g6rev
30		SEQ ID NO: 212 is the determined cDNA sequence for 8-b5fwd

	SEQ ID NO: 213 is the determined cDNA sequence for 8-b5re	v
	SEQ ID NO: 214 is the determined cDNA sequence for 8-b6fv	vd
	SEQ ID NO: 215 is the determined cDNA sequence for 8-b6 re	ev
	SEQ ID NO: 216 is the determined cDNA sequence for 8-d4fv	vd
5	SEQ ID NO: 217 is the determined cDNA sequence for 8-d9re	v
	SEQ ID NO: 218 is the determined cDNA sequence for 8-g3fv	vd
	SEQ ID NO: 219 is the determined cDNA sequence for 8-g3re	v
	SEQ ID NO: 220 is the determined cDNA sequence for 8-h11r	ev
	SEQ ID NO: 221 is the determined cDNA sequence for g-f12f	wđ
10	SEQ ID NO: 222 is the determined cDNA sequence for g-f3rev	V
	SEQ ID NO: 223 is the determined cDNA sequence for P509S	,
	SEQ ID NO: 224 is the determined cDNA sequence for P510S	٠.
	SEQ ID NO: 225 is the determined cDNA sequence for P703D	)E5
•	SEQ ID NO: 226 is the determined cDNA sequence for 9-A11	
15	SEQ ID NO: 227 is the determined cDNA sequence for 8-C6	
	SEQ ID NO: 228 is the determined cDNA sequence for 8-H7	
	SEQ ID NO: 229 is the determined cDNA sequence for JPTPN	113
	SEQ ID NO: 230 is the determined cDNA sequence for JPTPN	<b>114</b>
-	SEQ ID NO: 231 is the determined cDNA sequence for JPTPN	123
20	SEQ ID NO: 232 is the determined cDNA sequence for JPTPN	124
	SEQ ID NO: 233 is the determined cDNA sequence for JPTPN	125
	SEQ ID NO: 234 is the determined cDNA sequence for JPTPN	<b>130</b>
	SEQ ID NO: 235 is the determined cDNA sequence for JPTPN	134
	SEQ ID NO: 236 is the determined cDNA sequence for PTPN3	35
25	SEQ ID NO: 237 is the determined cDNA sequence for JPTPN	136
	SEQ ID NO: 238 is the determined cDNA sequence for JPTPN	[38
	SEQ ID NO: 239 is the determined cDNA sequence for JPTPN	[39
	SEQ ID NO: 240 is the determined cDNA sequence for JPTPN	ſ <b>40</b>
	SEQ ID NO: 241 is the determined cDNA sequence for JPTPN	[41
30	SEQ ID NO: 242 is the determined cDNA sequence for JPTPN	[42

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	SEQ ID NO: 243 is the determined cDNA sequence for JPTPN45
	SEQ ID NO: 244 is the determined cDNA sequence for JPTPN46
٠.	SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51
	SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56
	SEQ ID NO: 247 is the determined cDNA sequence for PTPN64
i	SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65
	SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67
•	SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76
	SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84
	SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85
	SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86
	SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87
* * *	SEQ ID NO: 255 is the determined cDNA sequence for JPTPN88
	SEQ ID NO: 256 is the determined cDNA sequence for JP1F1
	SEQ ID NO: 257 is the determined cDNA sequence for JP1F2
	SEQ ID NO: 258 is the determined cDNA sequence for JP1C2
· · · · · · · · · · · · · · · · · · ·	SEQ ID NO: 259 is the determined cDNA sequence for JP1B1
	SEQ ID NO: 260 is the determined cDNA sequence for JP1B2
, in the second	SEQ ID NO: 261 is the determined cDNA sequence for JP1D3
	SEQ ID NO: 262 is the determined cDNA sequence for JP1A4
	SEQ ID NO: 263 is the determined cDNA sequence for JP1F5
* *** ***	SEQ ID NO: 264 is the determined cDNA sequence for JP1E6
	SEQ ID NO: 265 is the determined cDNA sequence for JP1D6
ener eene	SEQ ID NO: 266 is the determined cDNA sequence for JP1B5
dollada.	SEQ ID NO: 267 is the determined cDNA sequence for JP1A6
e signist and a	SEQ ID NO: 268 is the determined cDNA sequence for JP1E8
9 (34), e (35).	SEQ ID NO: 269 is the determined cDNA sequence for JP1D7
F-4	SEQ ID NO: 270 is the determined cDNA sequence for JP1D9
	SEQ ID NO: 271 is the determined cDNA sequence for JP1C10
	SEQ ID NO: 272 is the determined cDNA sequence for JP1A9

* *	SEQ ID NO: 273 is the determined cDNA sequence for JP1F12
	SEQ ID NO: 274 is the determined cDNA sequence for JP1E12
	SEQ ID NO: 275 is the determined cDNA sequence for JP1D11
	SEQ ID NO: 276 is the determined cDNA sequence for JP1C11
5	SEQ ID NO: 277 is the determined cDNA sequence for JP1C12
•	SEQ ID NO: 278 is the determined cDNA sequence for JP1B12
	SEQ ID NO: 279 is the determined cDNA sequence for JP1A12
•	SEQ ID NO: 280 is the determined cDNA sequence for JP8G2
	SEQ ID NO: 281 is the determined cDNA sequence for JP8H1
10	SEQ ID NO: 282 is the determined cDNA sequence for JP8H2
1	SEQ ID NO: 283 is the determined cDNA sequence for JP8A3
•	SEQ ID NO: 284 is the determined cDNA sequence for JP8A4
d .	SEQ ID NO: 285 is the determined cDNA sequence for JP8C3
	SEQ ID NO: 286 is the determined cDNA sequence for JP8G4
15	SEQ ID NO: 287 is the determined cDNA sequence for JP8B6
	SEQ ID NO: 288 is the determined cDNA sequence for JP8D6
	SEQ ID NO: 289 is the determined cDNA sequence for JP8F5
	SEQ ID NO: 290 is the determined cDNA sequence for JP8A8
•	SEQ ID NO: 291 is the determined cDNA sequence for JP8C7
20	SEQ ID NO: 292 is the determined cDNA sequence for JP8D7
	SEQ ID NO: 293 is the determined cDNA sequence for P8D8
	SEQ ID NO: 294 is the determined cDNA sequence for JP8E7
	SEQ ID NO: 295 is the determined cDNA sequence for JP8F8
	SEQ ID NO: 296 is the determined cDNA sequence for JP8G8
25	SEQ ID NO: 297 is the determined cDNA sequence for JP8B10
	SEQ ID NO: 298 is the determined cDNA sequence for JP8C10
	SEQ ID NO: 299 is the determined cDNA sequence for JP8E9
	SEQ ID NO: 300 is the determined cDNA sequence for JP8E10
	SEQ ID NO: 301 is the determined cDNA sequence for JP8F9
30	SEQ ID NO: 302 is the determined cDNA sequence for JP8H9

	٠.,	SEQ ID NO: 303 is the determined cDNA sequence for JP8C12
		SEQ ID NO: 304 is the determined cDNA sequence for JP8E11
		SEQ ID NO: 305 is the determined cDNA sequence for JP8E12
		SEQ ID NO: 306 is the amino acid sequence for the peptide PS2#12
5		SEQ ID NO: 307 is the determined cDNA sequence for P711P
		SEQ ID NO: 308 is the determined cDNA sequence for P712P
_		SEQ ID NO: 309 is the determined cDNA sequence for CLONE23
	•	SEQ ID NO: 310 is the determined cDNA sequence for P774P
٠.		SEQ ID NO: 311 is the determined cDNA sequence for P775P
10		SEQ ID NO: 312 is the determined cDNA sequence for P715P
	2 - 1 - 0	SEQ ID NO: 313 is the determined cDNA sequence for P710P
	Sept.	SEQ ID NO: 314 is the determined cDNA sequence for P767P
		SEQ ID NO: 315 is the determined cDNA sequence for P768P
•		SEQ ID NO: 316-325 are the determined cDNA sequences of previously
15	isolated genes	en de la companya de
	*	SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5
		SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5
	, i	SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26
	· .	SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26
20		SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23
		SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23
		SEQ ID NO: 332 is the determined full length cDNA sequence for
	P509S	
	3698 G ±0	SEQ ID NO: 333 is the determined extended cDNA sequence for P707F
25		to as 11-C9)
	1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1	SEQ ID NO: 334 is the determined cDNA sequence for P714P
		SEQ ID NO: 335 is the determined cDNA sequence for P705P (also
	referred to as	9-F3) 9-F3)
		SEQ ID NO: 336 is the predicted amino acid sequence for P705P
RO		SEO ID NO: 337 is the amino acid sequence of the pentide P1S#10

1	SEQ ID NO: 338 is the amino acid sequence of the peptide p5
	SEQ ID NO: 339 is the predicted amino acid sequence of P509S
	SEQ ID NO: 340 is the determined cDNA sequence for P778P
	SEQ ID NO: 341 is the determined cDNA sequence for P786P
5	SEQ ID NO: 342 is the determined cDNA sequence for P789P
'	SEQ ID NO: 343 is the determined cDNA sequence for a clone showing
	homology to Homo sapiens MM46 mRNA
	SEQ ID NO: 344 is the determined cDNA sequence for a clone showing
	homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA
10	SEQ ID NO: 345 is the determined cDNA sequence for a clone showing
	homology to Homo sapiens mRNA for E-cadherin
•	SEQ ID NO: 346 is the determined cDNA sequence for a clone showing
	homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase
:	(SHMT)
15	SEQ ID NO: 347 is the determined cDNA sequence for a clone showing
	homology to Homo sapiens natural resistance-associated macrophage protein2
	(NRAMP2)
	SEQ ID NO: 348 is the determined cDNA sequence for a clone showing
	homology to Homo sapiens phosphoglucomutase-related protein (PGMRP)
20	SEQ ID NO: 349 is the determined cDNA sequence for a clone showing
	homology to Human mRNA for proteosome subunit p40
	SEQ ID NO: 350 is the determined cDNA sequence for P777P
	SEQ ID NO: 351 is the determined cDNA sequence for P779P
	SEQ ID NO: 352 is the determined cDNA sequence for P790P
25	SEQ ID NO: 353 is the determined cDNA sequence for P784P
	SEQ ID NO: 354 is the determined cDNA sequence for P776P
	SEQ ID NO: 355 is the determined cDNA sequence for P780P
	SEQ ID NO: 356 is the determined cDNA sequence for P544S
	SEQ ID NO: 357 is the determined cDNA sequence for P745S
30	SEQ ID NO: 358 is the determined cDNA sequence for P782P

	•
1	SEQ ID NO: 359 is the determined cDNA sequence for P783P
i	SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984
MAG.	SEQ ID NO: 361 is the determined cDNA sequence for P787P
4.	SEQ ID NO: 362 is the determined cDNA sequence for P788P
5	SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994
	SEQ ID NO: 364 is the determined cDNA sequence for P781P
	SEQ ID NO: 365 is the determined cDNA sequence for P785P
.277	SEQ ID NO: 366-375 are the determined cDNA sequences for splice
34-	variants of B305D.
10	SEQ ID NO: 376 is the predicted amino acid sequence encoded by the
	sequence of SEQ ID NO: 366.
- -	SEQ ID NO: 377 is the predicted amino acid sequence encoded by the
.,	sequence of SEQ ID NO: 372.
	SEQ ID NO: 378 is the predicted amino acid sequence encoded by the
15	sequence of SEQ ID NO: 373 Section 1997
	SEQ ID NO: 379 is the predicted amino acid sequence encoded by the
	sequence of SEQ ID NO: 374.
•	SEQ ID NO: 380 is the predicted amino acid sequence encoded by the
	sequence of SEQ ID NO: 375.
20	SEQ ID NO: 381 is the determined cDNA sequence for B716P.
	SEQ ID NO: 382 is the determined full-length cDNA sequence for
	P711P.
	SEQ ID NO: 383 is the predicted amino acid sequence for P711P.
per in	SEQ ID NO: 384 is the cDNA sequence for P1000C.
25	SEQ ID NO: 385 is the cDNA sequence for CGI-82.
·	SEQ ID NO:386 is the cDNA sequence for 23320.
	SEQ ID NO:387 is the cDNA sequence for CGI-69.
	SEQ ID NO:388 is the cDNA sequence for L-iditol-2-dehydrogenase.
	SEQ ID NO:389 is the cDNA sequence for 23379.
30	SEQ ID NO:390 is the cDNA sequence for 23381.

		SEQ ID NO:391 is the cDNA sequence for KIAA0122.
		SEQ ID NO:392 is the cDNA sequence for 23399.
		SEQ ID NO:393 is the cDNA sequence for a previously identified gene.
		SEQ ID NO:394 is the cDNA sequence for HCLBP.
5		SEQ ID NO:395 is the cDNA sequence for transglutaminase.
		SEQ ID NO:396 is the cDNA sequence for a previously identified gene.
	, f	SEQ ID NO:397 is the cDNA sequence for PAP.
• .	•	SEQ ID NO:398 is the cDNA sequence for Ets transcription factor
	PDEF.	
10		SEQ ID NO:399 is the cDNA sequence for hTGR.
		SEQ ID NO:400 is the cDNA sequence for KIAA0295.
		SEQ ID NO:401 is the cDNA sequence for 22545.
		SEQ ID NO:402 is the cDNA sequence for 22547.
•		SEQ ID NO:403 is the cDNA sequence for 22548.
15		SEQ ID NO:404 is the cDNA sequence for 22550.
	,	SEQ ID NO:405 is the cDNA sequence for 22551.
		SEQ ID NO:406 is the cDNA sequence for 22552.
		SEQ ID NO:407 is the cDNA sequence for 22553 (also known as
	P1020C).	
20		SEQ ID NO:408 is the cDNA sequence for 22558.
		SEQ ID NO:409 is the cDNA sequence for 22562.
		SEQ ID NO:410 is the cDNA sequence for 22565.
	•	SEQ ID NO:411 is the cDNA sequence for 22567.
		SEQ ID NO:412 is the cDNA sequence for 22568.
25		SEQ ID NO:413 is the cDNA sequence for 22570.
		SEQ ID NO:414 is the cDNA sequence for 22571.
		SEQ ID NO:415 is the cDNA sequence for 22572.
		SEQ ID NO:416 is the cDNA sequence for 22573.
		SEQ ID NO:417 is the cDNA sequence for 22573.
30		SEQ ID NO:418 is the cDNA sequence for 22575.

	SEQ ID NO:419 is the cDNA sequence for 22580
	SEQ ID NO:420 is the cDNA sequence for 22581
1850 ·-	SEQ ID NO:421 is the cDNA sequence for 22582
	SEQ ID NO:422 is the cDNA sequence for 22583
5	SEQ ID NO:423 is the cDNA sequence for 22584
ı	SEQ ID NO:424 is the cDNA sequence for 22585
	SEQ ID NO:425 is the cDNA sequence for 22586
	SEQ ID NO:426 is the cDNA sequence for 22587
	SEQ ID NO:427 is the cDNA sequence for 22588
10	SEQ ID NO:428 is the cDNA sequence for 22589
ti.	SEQ ID NO:429 is the cDNA sequence for 22590
	SEQ ID NO:430 is the cDNA sequence for 22591
	SEQ ID NO:431 is the cDNA sequence for 22592
•	SEQ ID NO:432 is the cDNA sequence for 22593
15	SEQ ID NO:433 is the cDNA sequence for 22594
	SEQ ID NO:434 is the cDNA sequence for 22595
	SEQ ID NO:435 is the cDNA sequence for 22596
· ·	SEQ ID NO:436 is the cDNA sequence for 22847
	SEQ ID NO:437 is the cDNA sequence for 22848
20	SEQ ID NO:438 is the cDNA sequence for 22849
s fr	SEQ ID NO:439 is the cDNA sequence for 22851
	SEQ ID NO:440 is the cDNA sequence for 22852
	SEQ ID NO:441 is the cDNA sequence for 22853
	SEQ ID NO:442 is the cDNA sequence for 22854
25	SEQ ID NO:443 is the cDNA sequence for 22855
	SEQ ID NO:444 is the cDNA sequence for 22856
•	SEQ ID NO:445 is the cDNA sequence for 22857
	SEQ ID NO:446 is the cDNA sequence for 23601
	SEQ ID NO:447 is the cDNA sequence for 23602
30	SEQ ID NO:448 is the cDNA sequence for 23605

SEQ ID NO:449 is the cDNA sequence for 23606. SEQ ID NO:450 is the cDNA sequence for 23612. SEQ ID NO:451 is the cDNA sequence for 23614. SEQ ID NO:452 is the cDNA sequence for 23618. SEQ ID NO:453 is the cDNA sequence for 23622. SEQ ID NO:454 is the cDNA sequence for folate hydrolase. SEQ ID NO:455 is the cDNA sequence for LIM protein. SEQ ID NO:456 is the cDNA sequence for a known gene. SEQ ID NO:457 is the cDNA sequence for a known gene. SEQ ID NO:458 is the cDNA sequence for a previously identified gene. 10 SEQ ID NO:459 is the cDNA sequence for 23045. SEQ ID NO:460 is the cDNA sequence for 23032. SEQ ID NO:461 is the cDNA sequence for clone 23054. SEQ ID NO:462-467 are cDNA sequences for known genes. 15 SEQ ID NO:468-471 are cDNA sequences for P710P. SEQ ID NO:472 is a cDNA sequence for P1001C. SEQ ID NO: 473 is the determined cDNA sequence for a first splice

SEQ ID NO: 474 is the determined cDNA sequence for a second splice variant of P775P (referred to as 19947).

variant of P775P (referred to as 27505).

SEQ ID NO: 475 is the determined cDNA sequence for a third splice variant of P775P (referred to as 19941).

SEQ ID NO: 476 is the determined cDNA sequence for a fourth splice variant of P775P (referred to as 19937).

SEQ ID NO: 477 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.

SEQ ID NO: 478 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.

SEQ ID NO: 479 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 475.

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SEQ ID NO: 480 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 481 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 482 is a third predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 483 is a fourth predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 484 is the first 30 amino acids of the *M. tuberculosis* 10 antigen Ra12.

SEQ ID NO: 485 is the PCR primer AW025.

SEQ ID NO: 486 is the PCR primer AW003.

SEQ ID NO: 487 is the PCR primer AW027.

SEQ ID NO: 488 is the PCR primer AW026.

SEQ ID NO: 489-501 are peptides employed in epitope mapping studies.

SEQ ID NO: 502 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody 20D4.

SEQ ID NO: 503 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody JA1.

SEQ ID NO: 504 & 505 are peptides employed in epitope mapping studies.

SEQ ID NO: 506 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 8H2.

SEQ ID NO: 507 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 7H8.

SEQ ID NO: 508 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 2D4.

SEQ ID NO: 509-522 are peptides employed in epitope mapping studies.

SEQ ID NO: 523 is a mature form of P703P used to raise antibodies

· 大大 大松 (18) and and an

30 against P703P.

SEQ ID NO: 524 is the putative full-length cDNA sequence of P703P.

SEQ ID NO: 525 is the predicted amino acid sequence encoded by SEQ

ID NO: 524.

SEQ ID NO: 526 is the full-length cDNA sequence for P790P.

SEQ ID NO: 527 is the predicted amino acid sequence for P790P.

SEQ ID NO: 528 & 529 are PCR primers.

SEQ ID NO: 530 is the cDNA sequence of a splice variant of SEQ ID

NO: 366.

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SEQ ID NO: 531 is the cDNA sequence of the open reading frame of

10 SEQ ID NO: 530.

SEQ ID NO: 532 is the predicted amino acid encoded by the sequence of SEQ ID NO: 531.

SEQ ID NO: 533 is the DNA sequence of a putative ORF of P775P.

SEQ ID NO: 534 is the predicted amino acid sequence encoded by SEQ

15 ID NO: 533.

SEQ ID NO: 535 is a first full-length cDNA sequence for P510S.

SEQ ID NO: 536 is a second full-length cDNA sequence for P510S.

SEQ ID NO: 537 is the predicted amino acid sequence encoded by SEQ

ID NO: 535.

20 SEQ ID NO: 538 is the predicted amino acid sequence encoded by SEQ

ID NO: 536.

SEO ID NO: 539 is the peptide P501S-370.

SEQ ID NO: 540 is the peptide P501S-376.

SEQ ID NO: 541-551 are epitopes of P501S.

25 SEQ ID NO: 552 is an extended cDNA sequence for P712P.

SEQ ID NO: 553-568 are the amino acid sequences encoded by predicted open reading frames within SEQ ID NO: 552.

SEQ ID NO: 569 is an extended cDNA sequence for P776P.

SEQ ID NO: 570 is the determined cDNA sequence for a splice variant 30 of P776P referred to as contig 6.

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SEQ ID NO: 571 is the determined cDNA sequence for a splice variant of P776P referred to as contig 7.

SEQ ID NO: 572 is the determined cDNA sequence for a splice variant of P776P referred to as contig 14.

SEQ ID NO: 573 is the amino acid sequence encoded by a first predicted ORF of SEQ ID NO: 570.

SEQ ID NO: 574 is the amino acid sequence encoded by a second predicted ORF of SEQ ID NO: 570.

SEQ ID NO: 575 is the amino acid sequence encoded by a predicted 10 ORF of SEQ ID NO: 571.

SEQ ID NO: 576-586 are amino acid sequences encoded by predicted ORFs of SEQ ID NO: 569.

SEQ ID NO: 587 is a DNA consensus sequence of the sequences of P767P and P777P.

SEQ ID NO: 588-590 are amino acid sequences encoded by predicted ORFs of SEQ ID NO: 587.

SEQ ID NO: 591 is an extended cDNA sequence for P1020C.

SEQ ID NO: 592 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: P1020C.

SEQ ID NO: 593 is a splice variant of P775P referred to as 50748.

SEQ ID NO: 594 is a splice variant of P775P referred to as 50717.

SEQ ID NO: 595 is a splice variant of P775P referred to as 45985.

SEQ ID NO: 596 is a splice variant of P775P referred to as 38769.

SEQ ID NO: 597 is a splice variant of P775P referred to as 37922.

SEQ ID NO: 598 is a splice variant of P510S referred to as 49274.

SEQ ID NO: 599 is a splice variant of P510S referred to as 39487.

SEQ ID NO: 600 is a splice variant of P504S referred to as 5167.16.

SEQ ID NO: 601 is a splice variant of P504S referred to as 5167.1.

SEQ ID NO: 602 is a splice variant of P504S referred to as 5163.46.

30 SEQ ID NO: 603 is a splice variant of P504S referred to as 5163.42.

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SEQ ID NO: 604 is a splice variant of P504S referred to as 5163.34.

SEQ ID NO: 605 is a splice variant of P504S referred to as 5163.17.

SEQ ID NO: 606 is a splice variant of P501S referred to as 10640.

SEQ ID NO: 607-615 are the sequences of PCR primers.

SEQ ID NO: 616 is the determined cDNA sequence of a fusion of P703P and PSA.

SEQ ID NO: 617 is the amino acid sequence of the fusion of P703P and

SEQ ID NO: 618 is the cDNA sequence of the gene DD3.

SEQ ID NO: 619 is an extended cDNA sequence for P714P.

SEQ ID NO: 620-622 are the cDNA sequences for splice variants of P704P.

SEQ ID NO: 623 is the cDNA sequence of a splice variant of P553S referred to as P553S-14.

SEQ ID NO: 624 is the cDNA sequence of a splice variant of P553S referred to as P553S-12.

SEQ ID NO: 625 is the cDNA sequence of a splice variant of P553S referred to as P553S-10.

SEQ ID NO: 626 is the cDNA sequence of a splice variant of P553S 20 referred to as P553S-6.

SEQ ID NO: 627 is the amino acid sequence encoded by SEQ ID NO:

SEQ ID NO: 628 is a first amino acid sequence encoded by SEQ ID NO: 623.

SEQ ID NO: 629 is a second amino acid sequence encoded by SEQ ID NO: 623.

SEQ ID NO: 630 is a first full-length cDNA sequence for prostate-specific transglutaminase gene (also referred to herein as P558S).

SEQ ID NO: 631 is a second full-length cDNA sequence for prostate-30 specific transglutaminase gene.

	٠.,	SEQ ID NO: 632 is the amino acid sequence encoded by the sequence of
	SEQ ID NO:	<b>630.</b>
* * <u>.</u>		SEQ ID NO: 633 is the amino acid sequence encoded by the sequence of
<del>.</del>	SEQ ID NO:	531.
5		SEQ ID NO: 634 is the full-length cDNA sequence for P788P.
		SEQ ID NO: 635 is the amino acid sequence encoded by SEQ ID NO:
	634.	
	•	SEQ ID NO: 636 is the determined cDNA sequence for a polymorphic
	variant of P78	8P.
10	. <sup>1</sup> : .	SEQ ID NO: 637 is the amino acid sequence encoded by SEQ ID NO:
<i>.</i>	<b>636.</b>	and the second of the second o
		SEQ ID NO: 638 is the amino acid sequence of peptide 4 from P703P.
e a y	5 p. €	SEQ ID NO: 639 is the cDNA sequence that encodes peptide 4 from
•	P703P.	Wind the result to suppose
15		SEQ ID NO: 640-655 are cDNA sequences encoding epitopes of P703P.
		SEQ ID NO: 656-671 are the amino acid sequences of epitopes of
	P703P.	the state of the s
		SEQ ID NO: 672 and 673 are PCR primers.
		SEQ ID NO: 674 is the cDNA sequence encoding an N-terminal portion
20	of P788P expr	ressed in E. coli.
17 %	** 3y	SEQ ID NO: 675 is the amino acid sequence of the N-terminal portion of
	P788P express	sed in E. coli.
ri, rij	O. 4 & 100 .	SEQ ID NO: 676 is the amino acid sequence of the M. tuberculosis
	antigen Ra12.	
. 25	l ou to reason.	SEQ ID NO: 677 and 678 are PCR primers.
		SEQ ID NO: 679 is the cDNA sequence for the Ra12-P510S-C
	construct.	a Altika ayan esi
		SEQ ID NO: 680 is the cDNA sequence for the P510S-C construct.
	$\omega_{i}^{\sigma}=1_{\sigma}$	SEQ ID NO: 681 is the cDNA sequence for the P510S-E3 construct.

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SEQ ID NO: 682 is the amino acid sequence for the Ra12-P510S-C construct.

SEQ ID NO: 683 is the amino acid sequence for the P510S-C construct.

SEQ ID NO: 684 is the amino acid sequence for the P510S-E3 construct.

SEQ ID NO: 685-690 are PCR primers.

SEQ ID NO: 691 is the cDNA sequence of the construct Ra12-P775P-ORF3.

SEQ ID NO: 692 is the amino acid sequence of the construct Ra12-P775P-ORF3.

SEQ ID NO: 693 and 694 are PCR primers.

SEQ ID NO: 695 is the determined amino acid sequence for a P703P His tag fusion protein.

SEQ ID NO: 696 is the determined cDNA sequence for a P703P His tag fusion protein.

15 SEQ ID NO: 697 and 698 are PCR primers.

SEQ ID NO: 699 is the determined amino acid sequence for a P705P His tag fusion protein.

SEQ ID NO: 700 is the determined cDNA sequence for a P705P His tag fusion protein.

SEQ ID NO: 701 and 702 are PCR primers.

SEQ ID NO: 703 is the determined amino acid sequence for a P711P His tag fusion protein.

SEQ ID NO: 704 is the determined cDNA sequence for a P711P His tag fusion protein.

SEQ ID NO: 705 is the amino acid sequence of the *M. tuberculosis* antigen Ra12.

SEQ ID NO: 706 and 707 are PCR primers.

SEQ ID NO: 708 is the determined cDNA sequence for the construct Ra12-P501S-E2.

,		SEQ ID NO: 709 is the determined amino acid sequence for the
·	construct Ra12	-P501S-E2.
<b>强神</b> 派		SEQ ID NO: 710 is the amino acid sequence for an epitope of P501S.
÷£.		SEQ ID NO: 711 is the DNA sequence encoding SEQ ID NO: 710.
٠ 5		SEQ ID NO: 712 is the amino acid sequence for an epitope of P501S.
		SEQ ID NO: 713 is the DNA sequence encoding SEQ ID NO: 712.
		SEQ ID NO: 714 is a peptide employed in epitope mapping studies.
.° ₽.	•	SEQ ID NO: 715 is the amino acid sequence for an epitope of P501S.
		SEQ ID NO: 716 is the DNA sequence encoding SEQ ID NO: 715.
10		SEQ ID NO: 717-719 are the amino acid sequences for CD4 epitopes of
. •	P501S.	Note that have the body to be thought to
,		SEQ ID NO: 720-722 are the DNA sequences encoding the sequences of
•	SEQ ID NO: 7	<b>17-719.</b> (# ) (4.546) (3.66) (# # ) # (4.546) (# ) # (5.66)
		SEQ ID NO: 723-734 are the amino acid sequences for putative CTL
15	epitopes of P70	OSP. The story of All State As Machine Control Control
	4,	SEQ ID NO: 735 is the full-length cDNA sequence for P789P.
		SEQ ID NO: 736 is the amino acid sequence encoded by SEQ ID NO:
	735.	
		SEQ ID NO: 737 is the determined full-length cDNA sequence for the
20	splice variant o	of P776P referred to as contig 6.
end to		SEQ ID NO: 738-739 are determined full-length cDNA sequences for
	the splice varia	nt of P776P referred to as contig 7.
		SEQ ID NO: 740-744 are amino acid sequences encoded by SEQ ID NO:
	737.	
.⊮25	SAM ASSO	SEQ ID NO: 745-750 are amino acid sequences encoded by the splice
	variant of P776	SP referred to as contig 7.
		SEQ ID NO: 751 is the full-length cDNA sequence for human
	transmembrane	protease serine 2.

SEQ ID NO: 752 is the amino acid sequence encoded by SEQ ID NO:

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SEQ ID NO: 753 is the cDNA sequence encoding the first 209 amino acids of human transmembrane protease serine 2.

SEQ ID NO: 754 is the first 209 amino acids of human transmembrane protease serine 2,

5 SEQ ID NO: 755 is the amino acid sequence of peptide 296-322 of P501S.

SEQ ID NO: 756-759 are PCR primers.

- SEQ ID NO: 760 is the determined cDNA sequence of the Vb chain of a T cell receptor for the P501S-specific T cell clone 4E5.
- SEQ ID NO: 761 is the determined cDNA sequence of the Va chain of a T cell receptor for the P501S-specific T cell clone 4E5.

SEQ ID NO: 762 is the amino acid sequence encoded by SEQ ID NO 760.

SEQ ID NO: 763 is the amino acid sequence encoded by SEQ ID NO

SEQ ID NO: 764 is the full-length open reading frame for P768P including stop codon.

SEQ ID NO: 765 is the full-length open reading frame for P768P without stop codon.

SEQ ID NO: 766 is the amino acid sequence encoded by SEQ ID NO: 765.

SEQ ID NO: 767-772 are the amino acid sequences for predicted domains of P768P.

SEQ ID NO: 773 is the full-length cDNA sequence of P835P.

SEQ ID NO: 774 is the cDNA sequence of the previously identified clone FLJ13581.

SEQ ID NO: 775 is the cDNA sequence of the open reading frame for P835P with stop codon.

SEQ ID NO: 776 is the cDNA sequence of the open reading frame for P835P without stop codon.

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SEQ ID NO: 777 is the full-length amino acid sequence for P835P.

SEQ ID NO: 778-785 are the amino acid sequences of extracellular and intracellular domains of P835P.

SEQ ID NO: 786 is the full-length cDNA sequence for P1000C.

SEQ ID NO: 787 is the cDNA sequence of the open reading frame for P1000C, including stop codon.

SEQ ID NO: 788 is the cDNA sequence of the open reading frame for P1000C, without stop codon.

SEQ ID NO: 789 is the full-length amino acid sequence for P1000C.

SEQ ID NO: 790 is amino acids 1-100 of SEQ ID NO: 789.

• SEQ ID NO: 791 is amino acids 100-492 of SEQ ID NO: 789.

SEQ ID NO: 792 is the amino acid sequence of an α prepro-P501S recombinant protein.

## 15 DETAILED DESCRIPTION OF THE INVENTION :

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The present invention is directed generally to compositions and their use in the therapy and diagnosis of cancer, particularly prostate cancer. As described further below, illustrative compositions of the present invention include, but are not restricted to, polypeptides, particularly immunogenic polypeptides, polynucleotides encoding such polypeptides, antibodies and other binding agents, antigen presenting cells (APCs) and immune system cells (e.g., T cells).

The practice of the present invention will employ, unless indicated specifically to the contrary, conventional methods of virology, immunology, microbiology, molecular biology and recombinant DNA techniques within the skill of the art, many of which are described below for the purpose of illustration. Such techniques are explained fully in the literature. See, e.g., Sambrook, et al. Molecular Cloning: A Laboratory Manual (2nd Edition, 1989); Maniatis et al. Molecular Cloning: A Laboratory Manual (1982); DNA Cloning: A Practical Approach, vol. I & II (D. Glover, ed.); Oligonucleotide Synthesis (N. Gait, ed., 1984); Nucleic Acid

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Hybridization (B. Hames & S. Higgins, eds., 1985); Transcription and Translation (B. Hames & S. Higgins, eds., 1984); Animal Cell Culture (R. Freshney, ed., 1986); Perbal, A Practical Guide to Molecular Cloning (1984).

All publications, patents and patent applications cited herein, whether supra or infra, are hereby incorporated by reference in their entirety.

As used in this specification and the appended claims, the singular forms "a," "an" and "the" include plural references unless the content clearly dictates offerwise.

## Polypeptide Compositions

As used herein, the term "polypeptide" " is used in its conventional meaning, i.e., as a sequence of amino acids. The polypeptides are not limited to a specific length of the product; thus, peptides, oligopeptides, and proteins are included within the definition of polypeptide, and such terms may be used interchangeably herein unless specifically indicated otherwise. This term also does not refer to or exclude post-expression modifications of the polypeptide, for example, glycosylations, acetylations, phosphorylations and the like, as well as other modifications known in the art, both naturally occurring and non-naturally occurring. A polypeptide may be an entire protein, or a subsequence thereof. Particular polypeptides of interest in the context of this invention are amino acid subsequences comprising epitopes, i.e., antigenic determinants substantially responsible for the immunogenic properties of a polypeptide and being capable of evoking an immune response.

Particularly illustrative polypeptides of the present invention comprise those encoded by a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 and 786-788, or a sequence that hybridizes under moderately stringent conditions, or, alternatively, under highly stringent conditions, to a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175,

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177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 and 786-788. In specific embodiments, the polypeptides of the invention comprise amino acid sequences as set forth in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 627-629, 632, 633, 635, 637, 638, 656-671, 675, 683, 684, 710, 712, 714, 715, 717-719, 723-734, 736, 740-750, 752, 754, 755, 766-772, 777-785 and 789-791.

The polypeptides of the present invention are sometimes herein referred to as prostate-specific proteins or prostate-specific polypeptides, as an indication that their identification has been based at least in part upon their increased levels of expression in prostate tissue samples. Thus, a "prostate-specific polypeptide" or "prostate-specific protein," refers generally to a polypeptide sequence of the present 15 invention, or a polynucleotide sequence encoding such a polypeptide, that is expressed in a substantial proportion of prostate tissue samples, for example preferably greater than about 20%, more preferably greater than about 30%, and most preferably greater than about 50% or more of prostate tissue samples tested, at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in other normal tissues, as determined using a representative assay provided herein. A prostatespecific polypeptide sequence of the invention, based upon its increased level of expression in tumor cells, has particular utility both as a diagnostic marker as well as a therapeutic target, as further described below.

The Color of the invention are immunogenic, i.e., they react detectably within an immunoassay (such as an ELISA or \_ 25 T-cell stimulation assay) with antisera and/or T-cells from a patient with prostate 的音音 cancer. Screening for immunogenic activity can be performed using techniques well known to the skilled artisan. For example, such screens can be performed using methods such as those described in Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. In one illustrative example, a 30

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polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, <sup>125</sup>I-labeled Protein A.

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As would be recognized by the skilled artisan, immunogenic portions of the polypeptides disclosed herein are also encompassed by the present invention. An "immunogenic portion," as used herein, is a fragment of an immunogenic polypeptide of the invention that itself is immunologically reactive (i.e., specifically binds) with the B-cells and/or T-cell surface antigen receptors that recognize the polypeptide. Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, Fundamental Immunology, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (i.e., they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well-known techniques.

In one preferred embodiment, an immunogenic portion of a polypeptide of the present invention is a portion that reacts with antisera and/or T-cells at a level that is not substantially less than the reactivity of the full-length polypeptide (e.g., in an ELISA and/or T-cell reactivity assay). Preferably, the level of immunogenic activity of the immunogenic portion is at least about 50%, preferably at least about 70% and most preferably greater than about 90% of the immunogenicity for the full-length polypeptide. In some instances, preferred immunogenic portions will be identified that have a level of immunogenic activity greater than that of the corresponding full-length polypeptide, e.g., having greater than about 100% or 150% or more immunogenic activity.

In certain other embodiments, illustrative immunogenic portions may include peptides in which an N-terminal leader sequence and/or transmembrane domain has been deleted. Other illustrative immunogenic portions will contain a small N-

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and/or C-terminal deletion (e.g., 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

In another embodiment, a polypeptide composition of the invention may 第一品 经证券 also comprise one or more polypeptides that are immunologically reactive with T cells and/or antibodies generated against a polypeptide of the invention, particularly a polypeptide having an amino acid sequence disclosed herein, or to an immunogenic fragment or variant thereof.

In another embodiment of the invention, polypeptides are provided that comprise one or more polypeptides that are capable of eliciting T cells and/or antibodies that are immunologically reactive with one or more polypeptides described herein, or one or more polypeptides encoded by contiguous nucleic acid sequences contained in the polynucleotide sequences disclosed herein, or immunogenic fragments or variants thereof, or to one or more nucleic acid sequences which hybridize to one or more of these sequences under conditions of moderate to high stringency.

The present invention, in another aspect, provides polypeptide fragments 15 comprising at least about 5, 10, 15, 20, 25, 50, or 100 contiguous amino acids, or more, including all intermediate lengths, of a polypeptide composition set forth herein, such as those set forth in SEO ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 20 573-586, 588-590, 592, 627-629, 632, 633, 635, 637, 638, 656-671, 675, 683, 684, 710, 712, 714, 715, 717-719, 723-734, 736, 740-750, 752, 754, 755, 766-772, 777-785 and 789-791, or those encoded by a polynucleotide sequence set forth in a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 25 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 and 786-788.

In another aspect, the present invention provides variants of the polypeptide compositions described herein. Polypeptide variants generally encompassed by the present invention will typically exhibit at least about 70/, 75%, 80%, 85%, 90%, 91 %, 92%, 93%, 94%, 95%, 96%, 97 %, 98%, or 99% or more identity

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(determined as described below), along its length, to a polypeptide sequence set forth herein.

In one preferred embodiment, the polypeptide fragments and variants provided by the present invention are immunologically reactive with an antibody and/or T-cell that reacts with a full-length polypeptide specifically set forth herein.

In another preferred embodiment, the polypeptide fragments and variants provided by the present invention exhibit a level of immunogenic activity of at least about 50%, preferably at least about 70%, and most preferably at least about 90% or more of that exhibited by a full-length polypeptide sequence specifically set forth herein.

A polypeptide "variant," as the term is used herein, is a polypeptide that typically differs from a polypeptide specifically disclosed herein in one or more substitutions, deletions, additions and/or insertions. Such variants may be naturally occurring or may be synthetically generated, for example, by modifying one or more of the above polypeptide sequences of the invention and evaluating their immunogenic activity as described herein using any of a number of techniques well known in the art.

For example, certain illustrative variants of the polypeptides of the invention include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other illustrative variants include variants in which a small portion (e.g., 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein.

In many instances, a variant will contain conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. As described above, modifications may be made in the structure of the polynucleotides and polypeptides of the present invention and still obtain a functional molecule that encodes a variant or derivative polypeptide with desirable characteristics, e.g., with immunogenic characteristics. When it is desired to alter the amino acid sequence of a polypeptide to create an equivalent, or

even an improved, immunogenic variant or portion of a polypeptide of the invention, one skilled in the art will typically change one or more of the codons of the encoding DNA sequence according to Table 1.

For example, certain amino acids may be substituted for other amino acids in a protein structure without appreciable loss of interactive binding capacity with structures such as, for example, antigen-binding regions of antibodies or binding sites on substrate molecules. Since it is the interactive capacity and nature of a protein that defines that protein's biological functional activity, certain amino acid sequence substitutions can be made in a protein sequence, and, of course, its underlying DNA coding sequence, and nevertheless obtain a protein with like properties. It is thus contemplated that various changes may be made in the peptide sequences of the disclosed compositions, or corresponding DNA sequences which encode said peptides without appreciable loss of their biological utility or activity.

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TABLE 1

Amino Acids			Codons					
Alanine	Ala	A	GCA	GCC	GCG	GCU		
Cysteine	Cys	C	UGC	UGU				
Aspartic acid	Asp	D	GAC	GAU				
Glutamic acid	Glu	E	GAA	GAG	,			
Phenylalanine	Phe	F	UUC	ບບບ່	'		·	
Glycine	Gly	G	GGA	GGC	GGG	GGU		
Histidine	His	H	CAC	CAU				
Isoleucine	Ile	1	AUA	AUC	AUU			
Lysine	Lys	K	AAA	AAG				
Leucine	Leu	: . <b>L</b>	UUA	UUG	CUA	CUC	CUG	CUU
Methionine	Met	<b>,M</b>	AUG	· ·			•	
Asparagine	Asn	N	AAC	AAU				
Proline	Pro	P	CCA	CCC	CCG	CCU		
Glutamine	Gln	Q	CAA	CAG				
Arginine	Arg	R	AGA	AGG	CGA	CGC	CGG	CGU
Serine	Ser	S	AGC	AGU	UCA	UCC	UCG	UCU
Threonine	Thr	T	ACA	ACC	ACG	ACU		
Valine	Val	$\mathbf{v}$	GUA	GUC	GUG	GUU	,	
Tryptophan	Trp	W	UGG		1			
Tyrosine	Tyr	Y	UAC	UAU			à	

In making such changes, the hydropathic index of amino acids may be considered. The importance of the hydropathic amino acid index in conferring interactive biologic function on a protein is generally understood in the art (Kyte and Doolittle, 1982, incorporated herein by reference). It is accepted that the relative hydropathic character of the amino acid contributes to the secondary structure of the resultant protein, which in turn defines the interaction of the protein with other molecules, for example, enzymes, substrates, receptors, DNA, antibodies, antigens, and the like. Each amino acid has been assigned a hydropathic index on the basis of its

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hydrophobicity and charge characteristics (Kyte and Doolittle, 1982). These values are: isoleucine (+4.5); valine (+4.2); leucine (+3.8); phenylalanine (+2.8); cysteine/cystine (+2.5); methionine (+1.9); alanine (+1.8); glycine (-0.4); threonine (-0.7); serine (-0.8); tryptophan (-0.9); tyrosine (-1.3); proline (-1.6); histidine (-3.2); glutamate (-3.5); glutamine (-3.5); asparagine (-3.5); lysine (-3.9); and arginine (-4.5).

It is known in the art that certain amino acids may be substituted by other amino acids having a similar hydropathic index or score and still result in a protein with similar biological activity, *i.e.* still obtain a biological functionally equivalent protein. In making such changes, the substitution of amino acids whose hydropathic indices are within ±2 is preferred, those within ±1 are particularly preferred, and those within ±0.5 are even more particularly preferred. It is also understood in the art that the substitution of like amino acids can be made effectively on the basis of hydrophilicity. U.S. Patent 4,554,101 (specifically incorporated herein by reference in its entirety), states that the greatest local average hydrophilicity of a protein, as governed by the hydrophilicity of its adjacent amino acids, correlates with a biological property of the protein.

As detailed in U. S. Patent 4,554,101, the following hydrophilicity values have been assigned to amino acid residues: arginine ( $\pm$ 3.0); lysine ( $\pm$ 3.0); aspartate ( $\pm$ 3.0  $\pm$  1); glutamate ( $\pm$ 3.0  $\pm$  1); serine ( $\pm$ 0.3); asparagine ( $\pm$ 0.2); glutamine ( $\pm$ 0.2); glycine (0); threonine ( $\pm$ 0.4); proline ( $\pm$ 0.5  $\pm$ 1); alanine ( $\pm$ 0.5); histidine ( $\pm$ 0.5); cysteine ( $\pm$ 1.0); methionine ( $\pm$ 1.3); valine ( $\pm$ 1.5); leucine ( $\pm$ 1.8); isoleucine ( $\pm$ 1.8); tyrosine ( $\pm$ 2.3); phenylalanine ( $\pm$ 2.5); tryptophan ( $\pm$ 3.4). It is understood that an amino acid can be substituted for another having a similar hydrophilicity value and still obtain a biologically equivalent, and in particular, an immunologically equivalent protein. In such changes, the substitution of amino acids whose hydrophilicity values are within  $\pm$ 2 is preferred, those within  $\pm$ 1 are particularly preferred, and those within  $\pm$ 0.5 are even more particularly preferred.

As outlined above, amino acid substitutions are generally therefore based on the relative similarity of the amino acid side-chain substituents, for example, their hydrophobicity, hydrophilicity, charge, size, and the like. Exemplary substitutions that take various of the foregoing characteristics into consideration are well known to those

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of skill in the art and include: arginine and lysine; glutamate and aspartate; serine and threonine; glutamine and asparagine; and valine, leucine and isoleucine.

In addition, any polynucleotide may be further modified to increase stability in vivo. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetylmethyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

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Amino acid substitutions may further be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydropathic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein, which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

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When comparing polypeptide sequences, two sequences are said to be "identical" if the sequence of amino acids in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

10 Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships.

15 In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenes pp. 626-645 Methods in Enzymology vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) CABIOS 5:151-153; Myers, E.W. and Muller W. (1988) CABIOS 4:11-17; Robinson, 20 E.D. (1971) Comb. Theor 11:105; Santou, N. Nes, M. (1987) Mol. Biol. Evol. 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) Proc. Natl. Acad., Sci. USA 80:726-730.

Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) Add. APL.

Math 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) J.

Mol. Biol. 48:443, by the search for similarity methods of Pearson and Lipman (1988)

Proc. Natl. Acad. Sci. USA 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics

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Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), or by inspection.

One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al. (1977) Nucl. Acids Res. 25:3389-3402 and Altschul et al. (1990) J. Mol. Biol. 215:403-410, respectively. BLAST and BLAST 2.0 can be used, for example with the parameters described herein, to determine percent sequence identity for the polynucleotides and polypeptides of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information. For amino acid sequences, a scoring matrix can be used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment.

In one preferred approach, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Within other illustrative embodiments, a polypeptide may be a fusion polypeptide that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known

tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the polypeptide or to enable the polypeptide to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags. which facilitate purification of the polypeptide.

Fusion polypeptides may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion polypeptide is expressed as a recombinant polypeptide, allowing the production of increased levels, relative to a non-fused polypeptide, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion polypeptide that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion polypeptide using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., Gene 40:39-46, 1985; Murphy et al.,

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Proc. Natl. Acad. Sci. USA 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

The fusion polypeptide can comprise a polypeptide as described herein together with an unrelated immunogenic protein, such as an immunogenic protein capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (see, for example, Stoute et al. New Engl. J. Med., 336:86-91, 1997).

In one preferred embodiment, the immunological fusion partner is derived from a Mycobacterium sp., such as a Mycobacterium tuberculosis-derived Ra12 fragment. Ra12 compositions and methods for their use in enhancing the expression and/or immunogenicity of heterologous polynucleotide/polypeptide sequences is described in U.S. Patent Application 60/158,585, the disclosure of which is incorporated herein by reference in its entirety. Briefly, Ra12 refers to a polynucleotide region that is a subsequence of a Mycobacterium tuberculosis MTB32A nucleic acid. MTB32A is a serine protease of 32 KD molecular weight encoded by a gene in virulent and avirulent strains of M. tuberculosis. The nucleotide sequence and amino acid sequence of MTB32A have been described (for example, U.S. Patent Application 60/158,585; see also, Skeiky et al., Infection and Immun. (1999) 67:3998-4007, incorporated herein by reference). C-terminal fragments of the MTB32A coding sequence express at high levels and remain as a soluble polypeptides throughout the purification process. Moreover, Ra12 may enhance the immunogenicity of heterologous

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immunogenic polypeptides with which it is fused. One preferred Ra12 fusion polypeptide comprises a 14 KD C-terminal fragment corresponding to amino acid residues 192 to 323 of MTB32A. Other preferred Ra12 polynucleotides generally comprise at least about 15 consecutive nucleotides, at least about 30 nucleotides, at least about 60 nucleotides, at least about 100 nucleotides, at least about 200 nucleotides, or at least about 300 nucleotides that encode a portion of a Ra12 polypeptide. Ra12 polynucleotides may comprise a native sequence (i.e., an endogenous sequence that encodes a Ra12 polypeptide or a portion thereof) or may comprise a variant of such a sequence. Ra12 polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the biological activity of the encoded fusion polypeptide is not substantially diminished, relative to a fusion polypeptide comprising a native Ra12 polypeptide. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native Ra12 polypeptide or a portion thereof.

Within other preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium Haemophilus influenza B (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (e.g., the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in E. coli (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemaglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine

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amidase known as amidase LYTA (encoded by the LytA gene; Gene 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of E. coli C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (see Biotechnology 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion polypeptide. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

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Yet another illustrative embodiment involves fusion polypeptides, and the polynucleotides encoding them, wherein the fusion partner comprises a targeting signal capable of directing a polypeptide to the endosomal/lysosomal compartment, as described in U.S. Patent No. 5,633,234. An immunogenic polypeptide of the invention, when fused with this targeting signal, will associate more efficiently with MHC class II molecules and thereby provide enhanced in vivo stimulation of CD4<sup>+</sup> T-cells specific for the polypeptide.

Polypeptides of the invention are prepared using any of a variety of well known synthetic and/or recombinant techniques, the latter of which are further described below. Polypeptides, portions and other variants generally less than about 150 amino acids can be generated by synthetic means, using techniques well known to those of ordinary skill in the art. In one illustrative example, such polypeptides are synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, J. Am. Chem. Soc. 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

In general, polypeptide compositions (including fusion polypeptides) of the invention are isolated. An "isolated" polypeptide is one that is removed from its 3.A. "

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original environment. For example, a naturally-occurring protein or polypeptide is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are also purified, e.g., are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure.

## Polynucleotide Compositions

The present invention, in other aspects, provides polynucleotide compositions. The terms "DNA" and "polynucleotide" are used essentially interchangeably herein to refer to a DNA molecule that has been isolated free of total genomic DNA of a particular species. "Isolated," as used herein, means that a polynucleotide is substantially away from other coding sequences, and that the DNA molecule does not contain large portions of unrelated coding DNA, such as large chromosomal fragments or other functional genes or polypeptide coding regions. Of course, this refers to the DNA molecule as originally isolated, and does not exclude genes or coding regions later added to the segment by the hand of man.

As will be understood by those skilled in the art, the polynucleotide compositions of this invention can include genomic sequences, extra-genomic and plasmid-encoded sequences and smaller engineered gene segments that express, or may be adapted to express, proteins, polypeptides, peptides and the like. Such segments may be naturally isolated, or modified synthetically by the hand of man.

As will be also recognized by the skilled artisan, polynucleotides of the invention may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules may include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

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Polynucleotides may comprise a native sequence (i.e., an endogenous sequence that encodes a polypeptide/protein of the invention or a portion thereof) or may comprise a sequence that encodes a variant or derivative, preferably an immunogenic variant or derivative, of such a sequence.

Therefore, according to another aspect of the present invention, 5 polynucleotide compositions are provided that comprise some or all of a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 and 10 786-788, complements of a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 and 786-788, and degenerate variants of a 15 polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 20 773-776 and 786-788. In certain preferred embodiments, the polynucleotide sequences set forth herein encode immunogenic polypeptides, as described above.

In other related embodiments, the present invention provides polynucleotide variants having substantial identity to the sequences disclosed herein in SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 and 786-788, for example those comprising at least 70% sequence identity, preferably at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% or higher, sequence identity compared to a polynucleotide sequence of this invention using the methods described herein, (e.g.,

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BLAST analysis using standard parameters, as described below). One skilled in this art will recognize that these values can be appropriately adjusted to determine corresponding identity of proteins encoded by two nucleotide sequences by taking into account codon degeneracy, amino acid similarity, reading frame positioning and the like.

Typically, polynucleotide variants will contain one or more substitutions, additions, deletions and/or insertions, preferably such that the immunogenicity of the polypeptide encoded by the variant polynucleotide is not substantially diminished relative to a polypeptide encoded by a polynucleotide sequence specifically set forth herein). The term "variants" should also be understood to encompasses homologous genes of xenogenic origin.

In additional embodiments, the present invention provides polynucleotide fragments comprising various lengths of contiguous stretches of sequence identical to, or complementary to, one or more of the sequences disclosed herein. For example, polynucleotides are provided by this invention that comprise at least about 10, 15, 20, 30, 40, 50, 75, 100, 150, 200, 300, 400, 500 or 1000 or more contiguous nucleotides of one or more of the sequences disclosed herein as well as all intermediate lengths there between. It will be readily understood that "intermediate lengths", in this context, means any length between the quoted values, such as 16, 17, 18, 19, etc.; 21, 22, 23, etc.; 30, 31, 32, etc.; 50, 51, 52, 53, etc.; 100, 101, 102, 103, etc.; 150, 151, 152, 153, etc.; including all integers through 200-500; 500-1,000, and the like.

In another embodiment of the invention, polynucleotide compositions are provided that are capable of hybridizing under moderate to high stringency conditions to a polynucleotide sequence provided herein, or a fragment thereof, or a complementary sequence thereof. Hybridization techniques are well known in the art of molecular biology. For purposes of illustration, suitable moderately stringent conditions for testing the hybridization of a polynucleotide of this invention with other polynucleotides include prewashing in a solution of 5 X SSC, 0.5 % SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-60°C, 5 X SSC, overnight; followed by washing twice at 65°C for

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20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1 & SDS. One skilled in the art will understand that the stringency of hybridization can be readily manipulated, such as by altering the salt content of the hybridization solution and/or the temperature at which the hybridization is performed. For example, in another embodiment, suitable highly stringent hybridization conditions include those described above, with the exception that the temperature of hybridization is increased, e.g., to 60-65°C or 65-70°C.

In certain preferred embodiments, the polynucleotides described above, e.g., polynucleotide variants, fragments and hybridizing sequences, encode polypeptides that are immunologically cross-reactive with a polypeptide sequence specifically set forth herein. In other preferred embodiments, such polynucleotides encode polypeptides that have a level of immunogenic activity of at least about 50%, preferably at least about 70%, and more preferably at least about 90% of that for a polypeptide sequence specifically set forth herein.

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The polynucleotides of the present invention, or fragments thereof, regardless of the length of the coding sequence itself, may be combined with other DNA sequences, such as promoters, polyadenylation signals, additional restriction enzyme sites, multiple cloning sites, other coding segments, and the like, such that their overall length may vary considerably. It is therefore contemplated that a nucleic acid fragment of almost any length may be employed, with the total length preferably being limited by the ease of preparation and use in the intended recombinant DNA protocol. For example, illustrative polynucleotide segments with total lengths of about 10,000, about 5000, about 3000, about 2,000, about 1,000, about 500, about 200, about 100, about 50 base pairs in length, and the like, (including all intermediate lengths) are contemplated to be useful in many implementations of this invention.

When comparing polynucleotide sequences, two sequences are said to be "identical" if the sequence of nucleotides in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison

window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, preferably 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins - Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenes pp. 626-645 Methods in Enzymology vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) CABIOS 5:151-153; Myers, E.W. and Muller W. (1988) CABIOS 4:11-17; Robinson, 15 E.D. (1971) Comb. Theor 11:105; Santou, N. Nes, M. (1987) Mol. Biol. Evol. 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) Numerical Taxonomy - the Principles and Practice of Numerical Taxonomy, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) Proc. Natl. Acad., Sci. USA 80:726-730.

Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) Add. APL. Math 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) J. Mol. Biol. 48:443, by the search for similarity methods of Pearson and Lipman (1988) Proc. Natl. Acad. Sci. USA 85: 2444, by computerized implementations of these galgorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), 25 or by inspection. 

One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al. (1977) Nucl. Acids Res. 25:3389-3402 and Altschul et al. (1990) J. Mol. Biol. 215:403-410, respectively. BLAST and BLAST

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2.0 can be used, for example with the parameters described herein, to determine percent sequence identity for the polynucleotides of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information. In one illustrative example, cumulative scores can be calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always >0) and N (penalty score for mismatching residues; always <0). Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1989) *Proc. Natl. Acad. Sci. USA* 89:10915) alignments, (B) of 50, expectation (E) of 10, M=5, N=4 and a comparison of both strands.

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Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide sequence in the comparison window may comprise additions or deletions (i.e., gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (i.e., the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides

that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Therefore, in another embodiment of the invention, a mutagenesis approach, such as site-specific mutagenesis, is employed for the preparation of immunogenic variants and/or derivatives of the polypeptides described herein. By this approach, specific modifications in a polypeptide sequence can be made through mutagenesis of the underlying polynucleotides that encode them. These techniques provides a straightforward approach to prepare and test sequence variants, for example, incorporating one or more of the foregoing considerations, by introducing one or more nucleotide sequence changes into the polynucleotide.

Site-specific mutagenesis allows the production of mutants through the use of specific oligonucleotide sequences which encode the DNA sequence of the desired mutation, as well as a sufficient number of adjacent nucleotides, to provide a primer sequence of sufficient size and sequence complexity to form a stable duplex on both sides of the deletion junction being traversed. Mutations may be employed in a selected polynucleotide sequence to improve, alter, decrease, modify, or otherwise change the properties of the polynucleotide itself, and/or alter the properties, activity, composition, stability, or primary sequence of the encoded polypeptide.

25 contemplate the mutagenesis of the disclosed polynucleotide sequences to alter one or more properties of the encoded polypeptide, such as the immunogenicity of a polypeptide vaccine. The techniques of site-specific mutagenesis are well-known in the art, and are widely used to create variants of both polypeptides and polynucleotides. For example, site-specific mutagenesis is often used to alter a specific portion of a DNA molecule. In such embodiments, a primer comprising typically about 14 to about 25

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nucleotides or so in length is employed, with about 5 to about 10 residues on both sides of the junction of the sequence being altered.

As will be appreciated by those of skill in the art, site-specific mutagenesis techniques have often employed a phage vector that exists in both a single stranded and double stranded form. Typical vectors useful in site-directed mutagenesis include vectors such as the M13 phage. These phage are readily commercially-available and their use is generally well-known to those skilled in the art. Double-stranded plasmids are also routinely employed in site directed mutagenesis that eliminates the step of transferring the gene of interest from a plasmid to a phage.

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In general, site-directed mutagenesis in accordance herewith is performed by first obtaining a single-stranded vector or melting apart of two strands of a double-stranded vector that includes within its sequence a DNA sequence that encodes the desired peptide. An oligonucleotide primer bearing the desired mutated sequence is prepared, generally synthetically. This primer is then annealed with the single-stranded vector, and subjected to DNA polymerizing enzymes such as *E. coli* polymerase I Klenow fragment, in order to complete the synthesis of the mutation-bearing strand. Thus, a heteroduplex is formed wherein one strand encodes the original non-mutated sequence and the second strand bears the desired mutation. This heteroduplex vector is then used to transform appropriate cells, such as *E. coli* cells, and clones are selected which include recombinant vectors bearing the mutated sequence arrangement.

The preparation of sequence variants of the selected peptide-encoding DNA segments using site-directed mutagenesis provides a means of producing potentially useful species and is not meant to be limiting as there are other ways in which sequence variants of peptides and the DNA sequences encoding them may be obtained. For example, recombinant vectors encoding the desired peptide sequence may be treated with mutagenic agents, such as hydroxylamine, to obtain sequence variants. Specific details regarding these methods and protocols are found in the teachings of Maloy et al., 1994; Segal, 1976; Prokop and Bajpai, 1991; Kuby, 1994; and Maniatis et al., 1982, each incorporated herein by reference, for that purpose.

As used herein, the term "oligonucleotide directed mutagenesis procedure" refers to template-dependent processes and vector-mediated propagation which result in an increase in the concentration of a specific nucleic acid molecule relative to its initial concentration, or in an increase in the concentration of a detectable signal, such as amplification. As used herein, the term "oligonucleotide directed mutagenesis procedure" is intended to refer to a process that involves the template-dependent extension of a primer molecule. The term template dependent process refers to nucleic acid synthesis of an RNA or a DNA molecule wherein the sequence of the newly synthesized strand of nucleic acid is dictated by the well-known rules of complementary base pairing (see, for example, Watson, 1987). Typically, vector mediated methodologies involve the introduction of the nucleic acid fragment into a DNA or RNA vector, the clonal amplification of the vector, and the recovery of the amplified nucleic acid fragment. Examples of such methodologies are provided by U. S. Patent No. 4,237,224, specifically incorporated herein by reference in its entirety.

In another approach for the production of polypeptide variants of the present invention, recursive sequence recombination, as described in U.S. Patent No. 5,837,458, may be employed. In this approach, iterative cycles of recombination and screening or selection are performed to "evolve" individual polynucleotide variants of the invention having, for example, enhanced immunogenic activity.

In other embodiments of the present invention, the polynucleotide sequences provided herein can be advantageously used as probes or primers for nucleic acid hybridization. As such, it is contemplated that nucleic acid segments that comprise a sequence region of at least about 15 contiguous nucleotides that has the same sequence as, or is complementary to, a 15 nucleotide long contiguous sequence disclosed herein will find particular utility. Longer contiguous identical or complementary sequences, e.g., those of about 20, 30, 40, 50, 100, 200, 500, 1000 (including all intermediate lengths) and even up to full length sequences will also be of use in certain embodiments.

The ability of such nucleic acid probes to specifically hybridize to a sequence of interest will enable them to be of use in detecting the presence of

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complementary sequences in a given sample. However, other uses are also envisioned, such as the use of the sequence information for the preparation of mutant species primers, or primers for use in preparing other genetic constructions.

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Polynucleotide molecules having sequence regions consisting of contiguous nucleotide stretches of 10-14, 15-20, 30, 50, or even of 100-200 nucleotides or so (including intermediate lengths as well), identical or complementary to a polynucleotide sequence disclosed herein, are particularly contemplated as hybridization probes for use in, e.g., Southern and Northern blotting. This would allow a gene product, or fragment thereof, to be analyzed, both in diverse cell types and also in various bacterial cells. The total size of fragment, as well as the size of the complementary stretch(es), will ultimately depend on the intended use or application of the particular nucleic acid segment. Smaller fragments will generally find use in hybridization embodiments, wherein the length of the contiguous complementary region may be varied, such as between about 15 and about 100 nucleotides, but larger contiguous complementarity stretches may be used, according to the length complementary sequences one wishes to detect.

The use of a hybridization probe of about 15-25 nucleotides in length allows the formation of a duplex molecule that is both stable and selective. Molecules having contiguous complementary sequences over stretches greater than 15 bases in length are generally preferred, though, in order to increase stability and selectivity of the hybrid, and thereby improve the quality and degree of specific hybrid molecules obtained. One will generally prefer to design nucleic acid molecules having genecomplementary stretches of 15 to 25 contiguous nucleotides, or even longer where desired.

25 Hybridization probes may be selected from any portion of any of the sequences disclosed herein. All that is required is to review the sequences set forth herein, or to any continuous portion of the sequences, from about 15-25 nucleotides in length up to and including the full length sequence, that one wishes to utilize as a probe or primer. The choice of probe and primer sequences may be governed by various

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factors. For example, one may wish to employ primers from towards the termini of the total sequence.

Small polynucleotide segments or fragments may be readily prepared by, for example, directly synthesizing the fragment by chemical means, as is commonly practiced using an automated oligonucleotide synthesizer. Also, fragments may be obtained by application of nucleic acid reproduction technology, such as the PCR<sup>TM</sup> technology of U. S. Patent 4,683,202 (incorporated herein by reference), by introducing selected sequences into recombinant vectors for recombinant production, and by other recombinant DNA techniques generally known to those of skill in the art of molecular biology.

The nucleotide sequences of the invention may be used for their ability to selectively form duplex molecules with complementary stretches of the entire gene or gene fragments of interest. Depending on the application envisioned, one will typically desire to employ varying conditions of hybridization to achieve varying degrees of selectivity of probe towards target sequence. For applications requiring high selectivity, one will typically desire to employ relatively stringent conditions to form the hybrids, e.g., one will select relatively low salt and/or high temperature conditions, such as provided by a salt concentration of from about 0.02 M to about 0.15 M salt at temperatures of from about 50°C to about 70°C. Such selective conditions tolerate little, if any, mismatch between the probe and the template or target strand, and would be particularly suitable for isolating related sequences.

Of course, for some applications, for example, where one desires to prepare mutants employing a mutant primer strand hybridized to an underlying template, less stringent (reduced stringency) hybridization conditions will typically be needed in order to allow formation of the heteroduplex. In these circumstances, one may desire to employ salt conditions such as those of from about 0.15 M to about 0.9 M salt, at temperatures ranging from about 20°C to about 55°C. Cross-hybridizing species can thereby be readily identified as positively hybridizing signals with respect to control hybridizations. In any case, it is generally appreciated that conditions can be rendered more stringent by the addition of increasing amounts of formamide, which serves to

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destabilize the hybrid duplex in the same manner as increased temperature. Thus, hybridization conditions can be readily manipulated, and thus will generally be a method of choice depending on the desired results.

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According to another embodiment of the present invention. polynucleotide compositions comprising antisense oligonucleotides are provided. Antisense oligonucleotides have been demonstrated to be effective and targeted inhibitors of protein synthesis, and, consequently, provide a therapeutic approach by which a disease can be treated by inhibiting the synthesis of proteins that contribute to the disease. The efficacy of antisense oligonucleotides for inhibiting protein synthesis is well established. For example, the synthesis of polygalactauronase and the muscarine type 2 acetylcholine receptor are inhibited by antisense oligonucleotides directed to their respective mRNA sequences (U. S. Patent 5,739,119 and U. S. Patent 5,759,829). Further, examples of antisense inhibition have been demonstrated with the nuclear protein cyclin, the multiple drug resistance gene (MDG1), ICAM-1, E-selectin, STK-1, striatal GABAA receptor and human EGF (Jaskulski et al., Science. 1988 Jun 10;240(4858):1544-6; Vasanthakumar and Ahmed, Cancer Commun. 1989;1(4):225-32; Peris et al., Brain Res Mol Brain Res. 1998 Jun 15;57(2):310-20; U. S. Patent 5,801,154; U.S. Patent 5,789,573; U.S. Patent 5,718,709 and U.S. Patent 5,610,288). Antisense constructs have also been described that inhibit and can be used to treat a variety of abnormal cellular proliferations, e.g. cancer (U. S. Patent 5,747,470; U. S. Patent 5,591,317 and U. S. Patent 5,783,683).

Therefore, in certain embodiments, the present invention provides oligonucleotide sequences that comprise all, or a portion of, any sequence that is capable of specifically binding to polynucleotide sequence described herein, or a complement thereof. In one embodiment, the antisense oligonucleotides comprise DNA or derivatives thereof. In another embodiment, the oligonucleotides comprise RNA or derivatives thereof. In a third embodiment, the oligonucleotides are modified DNAs comprising a phosphorothicated modified backbone. In a fourth embodiment, the oligonucleotide sequences comprise peptide nucleic acids or derivatives thereof. In each case, preferred compositions comprise a sequence region that is complementary,

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and more preferably substantially-complementary, and even more preferably, completely complementary to one or more portions of polynucleotides disclosed herein. Selection of antisense compositions specific for a given gene sequence is based upon analysis of the chosen target sequence and determination of secondary structure, T<sub>m</sub>, binding energy, and relative stability. Antisense compositions may be selected based upon their relative inability to form dimers, hairpins, or other secondary structures that would reduce or prohibit specific binding to the target mRNA in a host cell. Highly preferred target regions of the mRNA, are those which are at or near the AUG translation initiation codon, and those sequences which are substantially complementary to 5' regions of the mRNA. These secondary structure analyses and target site selection considerations can be performed, for example, using v.4 of the OLIGO primer analysis software and/or the BLASTN 2.0.5 algorithm software (Altschul *et al.*, Nucleic Acids Res. 1997 Sep 1;25(17):3389-402).

The use of an antisense delivery method employing a short peptide vector, termed MPG (27 residues), is also contemplated. The MPG peptide contains a hydrophobic domain derived from the fusion sequence of HIV gp41 and a hydrophilic domain from the nuclear localization sequence of SV40 T-antigen (Morris et al., Nucleic Acids Res. 1997 Jul 15;25(14):2730-6). It has been demonstrated that several molecules of the MPG peptide coat the antisense oligonucleotides and can be delivered into cultured mammalian cells in less than 1 hour with relatively high efficiency (90%). Further, the interaction with MPG strongly increases both the stability of the oligonucleotide to nuclease and the ability to cross the plasma membrane.

According to another embodiment of the invention, the polynucleotide compositions described herein are used in the design and preparation of ribozyme molecules for inhibiting expression of the tumor polypeptides and proteins of the present invention in tumor cells. Ribozymes are RNA-protein complexes that cleave nucleic acids in a site-specific fashion. Ribozymes have specific catalytic domains that possess endonuclease activity (Kim and Cech, Proc Natl Acad Sci U S A. 1987 Dec;84(24):8788-92; Forster and Symons, Cell. 1987 Apr 24;49(2):211-20). For example, a large number of ribozymes accelerate phosphoester transfer reactions with a

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high degree of specificity, often cleaving only one of several phosphoesters in an oligonucleotide substrate (Cech et al., Cell. 1981 Dec;27(3 Pt 2):487-96; Michel and Westhof, J Mol Biol. 1990 Dec 5;216(3):585-610; Reinhold-Hurek and Shub, Nature. 1992 May 14;357(6374):173-6). This specificity has been attributed to the requirement that the substrate bind via specific base-pairing interactions to the internal guide sequence ("IGS") of the ribozyme prior to chemical reaction.

Six basic varieties of naturally-occurring enzymatic RNAs are known presently. Each can catalyze the hydrolysis of RNA phosphodiester bonds in trans (and thus can cleave other RNA molecules) under physiological conditions. In general, enzymatic nucleic acids act by first binding to a target RNA. Such binding occurs through the target binding portion of a enzymatic nucleic acid which is held in close proximity to an enzymatic portion of the molecule that acts to cleave the target RNA. Thus, the enzymatic nucleic acid first recognizes and then binds a target RNA through complementary base-pairing, and once bound to the correct site, acts enzymatically to cut the target RNA. Strategic cleavage of such a target RNA will destroy its ability to direct synthesis of an encoded protein. After an enzymatic nucleic acid has bound and cleaved its RNA target, it is released from that RNA to search for another target and can repeatedly bind and cleave new targets.

technologies, such as antisense technology (where a nucleic acid molecule simply binds to a nucleic acid target to block its translation) since the concentration of ribozyme necessary to affect a therapeutic treatment is lower than that of an antisense oligonucleotide. This advantage reflects the ability of the ribozyme to act enzymatically. Thus, a single ribozyme molecule is able to cleave many molecules of target RNA. In addition, the ribozyme is a highly specific inhibitor, with the specificity of inhibition depending not only on the base pairing mechanism of binding to the target RNA, but also on the mechanism of target RNA cleavage. Single mismatches, or base-substitutions, near the site of cleavage can completely eliminate catalytic activity of a ribozyme. Similar mismatches in antisense molecules do not prevent their action (Woolf et al., Proc Natl Acad Sci U S A. 1992 Aug 15;89(16):7305-9). Thus, the

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specificity of action of a ribozyme is greater than that of an antisense oligonucleotide binding the same RNA site.

The enzymatic nucleic acid molecule may be formed in a hammerhead. hairpin, a hepatitis δ virus, group I intron or RNaseP RNA (in association with an RNA guide sequence) or Neurospora VS RNA motif. Examples of hammerhead motifs are described by Rossi et al. Nucleic Acids Res. 1992 Sep 11;20(17):4559-65. Examples of hairpin motifs are described by Hampel et al. (Eur. Pat. Appl. Publ. No. EP 0360257), Hampel and Tritz, Biochemistry 1989 Jun 13;28(12):4929-33; Hampel et al., Nucleic Acids Res. 1990 Jan 25;18(2):299-304 and U. S. Patent 5,631,359. An example of the hepatitis δ virus motif is described by Perrotta and Been, Biochemistry. 1992 Dec 1;31(47):11843-52; an example of the RNaseP motif is described by Guerrier-Takada et al., Cell. 1983 Dec;35(3 Pt 2):849-57; Neurospora VS RNA ribozyme motif is described by Collins (Saville and Collins, Cell. 1990 May 18;61(4):685-96; Saville and Collins, Proc Natl Acad Sci U S A. 1991 Oct 1;88(19):8826-30; Collins and Olive, Biochemistry. 1993 Mar 23;32(11):2795-9); and an example of the Group I intron is described in (U. S. Patent 4,987,071). All that is important in an enzymatic nucleic acid molecule of this invention is that it has a specific substrate binding site which is complementary to one or more of the target gene RNA regions, and that it have nucleotide sequences within or surrounding that substrate binding site which impart an 20 RNA cleaving activity to the molecule. Thus the ribozyme constructs need not be limited to specific motifs mentioned herein.

Ribozymes may be designed as described in Int. Pat. Appl. Publ. No. j 31 ke WO 93/23569 and Int. Pat. Appl. Publ. No. WO 94/02595, each specifically incorporated herein by reference) and synthesized to be tested in vitro and in vivo, as 25 described. Such ribozymes can also be optimized for delivery. While specific examples are provided, those in the art will recognize that equivalent RNA targets in other species can be utilized when necessary.

Ribozyme activity can be optimized by altering the length of the ribozyme binding arms, or chemically synthesizing ribozymes with modifications that prevent their degradation by serum ribonucleases (see e.g., Int. Pat. Appl. Publ. No. WO

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92/07065; Int. Pat. Appl. Publ. No. WO 93/15187; Int. Pat. Appl. Publ. No. WO 91/03162; Eur. Pat. Appl. Publ. No. 92110298.4; U. S. Patent 5,334,711; and Int. Pat. Appl. Publ. No. WO 94/13688, which describe various chemical modifications that can be made to the sugar moieties of enzymatic RNA molecules), modifications which enhance their efficacy in cells, and removal of stem II bases to shorten RNA synthesis times and reduce chemical requirements.

Sullivan et al. (Int. Pat. Appl. Publ. No. WO 94/02595) describes the general methods for delivery of enzymatic RNA molecules. Ribozymes may be administered to cells by a variety of methods known to those familiar to the art, including, but not restricted to, encapsulation in liposomes, by iontophoresis, or by incorporation into other vehicles, such as hydrogels, cyclodextrins, biodegradable nanocapsules, and bioadhesive microspheres. For some indications, ribozymes may be directly delivered ex vivo to cells or tissues with or without the aforementioned vehicles. Alternatively, the RNA/vehicle combination may be locally delivered by direct inhalation, by direct injection or by use of a catheter, infusion pump or stent. Other routes of delivery include, but are not limited to, intravascular, intramuscular, subcutaneous or joint injection, aerosol inhalation, oral (tablet or pill form), topical, systemic, ocular, intraperitoneal and/or intrathecal delivery. More detailed descriptions of ribozyme delivery and administration are provided in Int. Pat. Appl. Publ. No. WO 94/02595 and Int. Pat. Appl. Publ. No. WO 93/23569, each specifically incorporated herein by reference.

Another means of accumulating high concentrations of a ribozyme(s) within cells is to incorporate the ribozyme-encoding sequences into a DNA expression vector. Transcription of the ribozyme sequences are driven from a promoter for eukaryotic RNA polymerase I (pol I), RNA polymerase II (pol II), or RNA polymerase III (pol III). Transcripts from pol II or pol III promoters will be expressed at high levels in all cells; the levels of a given pol II promoter in a given cell type will depend on the nature of the gene regulatory sequences (enhancers, silencers, etc.) present nearby. Prokaryotic RNA polymerase promoters may also be used, providing that the prokaryotic RNA polymerase enzyme is expressed in the appropriate cells Ribozymes

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expressed from such promoters have been shown to function in mammalian cells. Such transcription units can be incorporated into a variety of vectors for introduction into mammalian cells, including but not restricted to, plasmid DNA vectors, viral DNA vectors (such as adenovirus or adeno-associated vectors), or viral RNA vectors (such as retroviral, semliki forest virus, sindbis virus vectors).

In another embodiment of the invention, peptide nucleic acids (PNAs) compositions are provided. PNA is a DNA mimic in which the nucleobases are attached to a pseudopeptide backbone (Good and Nielsen, Antisense Nucleic Acid Drug Dev. 1997 7(4) 431-37). PNA is able to be utilized in a number methods that traditionally have used RNA or DNA. Often PNA sequences perform better in techniques than the corresponding RNA or DNA sequences and have utilities that are not inherent to RNA or DNA. A review of PNA including methods of making, characteristics of, and methods of using, is provided by Corey (*Trends Biotechnol* 1997 Jun;15(6):224-9). As such, in certain embodiments, one may prepare PNA sequences that are complementary to one or more portions of the ACE mRNA sequence, and such PNA compositions may be used to regulate, alter, decrease, or reduce the translation of ACE-specific mRNA, and thereby alter the level of ACE activity in a host cell to which such PNA compositions have been administered.

phosphodiester backbone of DNA (Nielsen et al., Science 1991 Dec 6;254(5037):1497-500; Hanvey et al., Science. 1992 Nov 27;258(5087):1481-5; Hyrup and Nielsen, Bioorg Med Chem. 1996 Jan;4(1):5-23). This chemistry has three important consequences: firstly, in contrast to DNA or phosphorothioate oligonucleotides, PNAs are neutral molecules; secondly, PNAs are achiral, which avoids the need to develop a stereoselective synthesis; and thirdly, PNA synthesis uses standard Boc or Fmoc protocols for solid-phase peptide synthesis, although other methods, including a modified Merrifield method, have been used.

PNA monomers or ready-made oligomers are commercially available from PerSeptive Biosystems (Framingham, MA). PNA syntheses by either Boc or 30 Fmoc protocols are straightforward using manual or automated protocols (Norton et al.,

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Bioorg Med Chem. 1995 Apr;3(4):437-45). The manual protocol lends itself to the production of chemically modified PNAs or the simultaneous synthesis of families of closely related PNAs.

As with peptide synthesis, the success of a particular PNA synthesis will depend on the properties of the chosen sequence. For example, while in theory PNAs can incorporate any combination of nucleotide bases, the presence of adjacent purines can lead to deletions of one or more residues in the product. In expectation of this difficulty, it is suggested that, in producing PNAs with adjacent purines, one should repeat the coupling of residues likely to be added inefficiently. This should be followed by the purification of PNAs by reverse-phase high-pressure liquid chromatography, providing yields and purity of product similar to those observed during the synthesis of peptides.

Modifications of PNAs for a given application may be accomplished by coupling amino acids during solid-phase synthesis or by attaching compounds that contain a carboxylic acid group to the exposed N-terminal amine. Alternatively, PNAs 15 can be modified after synthesis by coupling to an introduced lysine or cysteine. The ease with which PNAs can be modified facilitates optimization for better solubility or for specific functional requirements. Once synthesized, the identity of PNAs and their derivatives can be confirmed by mass spectrometry. Several studies have made and utilized modifications of PNAs (for example, Norton et al., Bioorg Med Chem. 1995 20 Apr;3(4):437-45; Petersen et al., J Pept Sci. 1995 May-Jun;1(3):175-83; Orum et al., Biotechniques. 1995 Sep;19(3):472-80; Footer et al., Biochemistry. 1996 Aug 20;35(33):10673-9; Griffith et al., Nucleic Acids Res. 1995 Aug 11;23(15):3003-8; Pardridge et al., Proc Natl Acad Sci U S A. 1995 Jun 6;92(12):5592-6; Boffa et al., Proc Natl Acad Sci U S A. 1995 Mar 14;92(6):1901-5; Gambacorti-Passerini et al., 25 Blood. 1996 Aug 15;88(4):1411-7; Armitage et al., Proc Natl Acad Sci U S A. 1997 Nov 11;94(23):12320-5; Seeger et al., Biotechniques. 1997 Sep;23(3):512-7). U.S. Patent No. 5,700,922 discusses PNA-DNA-PNA chimeric molecules and their uses in diagnostics, modulating protein in organisms, and treatment of conditions susceptible to 30 therapeutics.

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Methods of characterizing the antisense binding properties of PNAs are discussed in Rose (Anal Chem. 1993 Dec 15;65(24):3545-9) and Jensen *et al.* (Biochemistry. 1997 Apr 22;36(16):5072-7). Rose uses capillary gel electrophoresis to determine binding of PNAs to their complementary oligonucleotide, measuring the relative binding kinetics and stoichiometry. Similar types of measurements were made by Jensen *et al.* using BIAcore<sup>TM</sup> technology.

Other applications of PNAs that have been described and will be apparent to the skilled artisan include use in DNA strand invasion, antisense inhibition, mutational analysis, enhancers of transcription, nucleic acid purification, isolation of transcriptionally active genes, blocking of transcription factor binding, genome cleavage, biosensors, *in situ* hybridization, and the like.

## Polynucleotide Identification, Characterization and Expression

Polynucleotide compositions of the present invention may be identified, prepared and/or manipulated using any of a variety of well established techniques (see generally, Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989, and other like references). For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (i.e., expression that is at least two fold greater in a tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed, for example, using the microarray technology of Affymetrix, Inc. (Santa Clara, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., Proc. Natl. Acad. Sci. USA 94:2150-2155, 1997). Alternatively, polynucleotides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as tumor cells.

Many template dependent processes are available to amplify a target sequences of interest present in a sample. One of the best known amplification methods is the polymerase chain reaction (PCR<sup>TM</sup>) which is described in detail in U.S. Patent Nos. 4,683,195, 4,683,202 and 4,800,159, each of which is incorporated herein by

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reference in its entirety. Briefly, in PCR<sup>TM</sup>, two primer sequences are prepared which are complementary to regions on opposite complementary strands of the target sequence. An excess of deoxynucleoside triphosphates is added to a reaction mixture along with a DNA polymerase (e.g., Taq polymerase). If the target sequence is present in a sample, the primers will bind to the target and the polymerase will cause the primers to be extended along the target sequence by adding on nucleotides. By raising and lowering the temperature of the reaction mixture, the extended primers will dissociate from the target to form reaction products, excess primers will bind to the target and to the reaction product and the process is repeated. Preferably reverse transcription and PCR<sup>TM</sup> amplification procedure may be performed in order to quantify the amount of mRNA amplified. Polymerase chain reaction methodologies are well known in the art.

Any of a number of other template dependent processes, many of which are variations of the PCR TM amplification technique, are readily known and available in the art. Illustratively, some such methods include the ligase chain reaction (referred to 15 as LCR), described, for example, in Eur. Pat. Appl. Publ. No. 320,308 and U.S. Patent No. 4,883,750; Qbeta Replicase, described in PCT Intl. Pat. Appl. Publ. No. PCT/US87/00880; Strand Displacement Amplification (SDA) and Repair Chain Reaction (RCR). Still other amplification methods are described in Great Britain Pat. 20 Appl. No. 2 202 328, and in PCT Intl. Pat. Appl. Publ. No. PCT/US89/01025. Other nucleic acid amplification procedures include transcription-based amplification systems (TAS) (PCT Intl. Pat. Appl. Publ. No. WO 88/10315), including nucleic acid sequence based amplification (NASBA) and 3SR. Eur. Pat. Appl. Publ. No. 329,822 describes a nucleic acid amplification process involving cyclically synthesizing single-stranded RNA ("ssRNA"), ssDNA, and double-stranded DNA (dsDNA). PCT Intl. Pat. Appl. 25 Publ. No. WO 89/06700 describes a nucleic acid sequence amplification scheme based on the hybridization of a promoter/primer sequence to a target single-stranded DNA ("ssDNA") followed by transcription of many RNA copies of the sequence. Other amplification methods such as "RACE" (Frohman, 1990), and "one-sided PCR" (Ohara, 1989) are also well-known to those of skill in the art. 30

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An amplified portion of a polynucleotide of the present invention may be used to isolate a full length gene from a suitable library (e.g., a tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with <sup>32</sup>P) using well known techniques. A bacterial or bacteriophage library is then generally screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences can then assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

Alternatively, amplification techniques, such as those described above, tarental of the can be useful for obtaining a full length coding sequence from a partial cDNA sequence. One such amplification technique is inverse PCR (see Triglia et al., Nucl. Acids Res. 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of

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amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al.; PCR Methods Applic. 1:111-19, 1991) and walking PCR (Parker et al.; Nucl. Acids. Res. 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (e.g., NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

In other embodiments of the invention, polynucleotide sequences or fragments thereof which encode polypeptides of the invention, or fusion proteins or functional equivalents thereof, may be used in recombinant DNA molecules to direct expression of a polypeptide in appropriate host cells. Due to the inherent degeneracy of the genetic code, other DNA sequences that encode substantially the same or a functionally equivalent amino acid sequence may be produced and these sequences may be used to clone and express a given polypeptide.

As will be understood by those of skill in the art, it may be advantageous in some instances to produce polypeptide-encoding nucleotide sequences possessing non-naturally occurring codons. For example, codons preferred by a particular prokaryotic or eukaryotic host can be selected to increase the rate of protein expression or to produce a recombinant RNA transcript having desirable properties, such as a half-life which is longer than that of a transcript generated from the naturally occurring sequence.

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Moreover, the polynucleotide sequences of the present invention can be engineered using methods generally known in the art in order to alter polypeptide encoding sequences for a variety of reasons, including but not limited to, alterations which modify the cloning, processing, and/or expression of the gene product. For example, DNA shuffling by random fragmentation and PCR reassembly of gene fragments and synthetic oligonucleotides may be used to engineer the nucleotide sequences. In addition, site-directed mutagenesis may be used to insert new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, or introduce mutations, and so forth.

In another embodiment of the invention, natural, modified, or recombinant nucleic acid sequences may be ligated to a heterologous sequence to encode a fusion protein. For example, to screen peptide libraries for inhibitors of polypeptide activity, it may be useful to encode a chimeric protein that can be recognized by a commercially available antibody. A fusion protein may also be engineered to contain a cleavage site located between the polypeptide-encoding sequence and the heterologous protein sequence, so that the polypeptide may be cleaved and purified away from the heterologous moiety.

Sequences encoding a desired polypeptide may be synthesized, in whole or in part, using chemical methods well known in the art (see Caruthers, M. H. et al. (1980) Nucl. Acids Res. Symp. Ser. 215-223, Horn, T. et al. (1980) Nucl. Acids Res. Symp. Ser. 225-232). Alternatively, the protein itself may be produced using chemical methods to synthesize the amino acid sequence of a polypeptide, or a portion thereof. For example, peptide synthesis can be performed using various solid-phase techniques (Roberge, J. Y. et al. (1995) Science 269:202-204) and automated synthesis may be achieved, for example, using the ABI 431A Peptide Synthesizer (Perkin Elmer, Palo Alto, CA).

A newly synthesized peptide may be substantially purified by preparative high performance liquid chromatography (e.g., Creighton, T. (1983) Proteins, Structures and Molecular Principles, WH Freeman and Co., New York, N.Y.) or other comparable techniques available in the art. The composition of the synthetic peptides may be

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confirmed by amino acid analysis or sequencing (e.g., the Edman degradation procedure). Additionally, the amino acid sequence of a polypeptide, or any part thereof, may be altered during direct synthesis and/or combined using chemical methods with sequences from other proteins, or any part thereof, to produce a variant polypeptide.

In order to express a desired polypeptide, the nucleotide sequences encoding the polypeptide, or functional equivalents, may be inserted into appropriate expression vector, i.e., a vector which contains the necessary elements for the transcription and translation of the inserted coding sequence. Methods which are well known to those skilled in the art may be used to construct expression vectors containing sequences encoding a polypeptide of interest and appropriate transcriptional and translational control elements. These methods include in vitro recombinant DNA techniques, synthetic techniques, and in vivo genetic recombination. Such techniques are described, for example, in Sambrook, J. et al. (1989) Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Press, Plainview, N.Y., and Ausubel, F. M. et al. (1989) Current Protocols in Molecular Biology, John Wiley & Sons, New York. N.Y.

A variety of expression vector/host systems may be utilized to contain and express polynucleotide sequences. These include, but are not limited to, microorganisms such as bacteria transformed with recombinant bacteriophage, plasmid, or cosmid DNA expression vectors; yeast transformed with yeast expression vectors; insect cell systems infected with virus expression vectors (e.g., baculovirus); plant cell systems transformed with virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or with bacterial expression vectors (e.g., Ti or pBR322 plasmids); or animal cell systems.

The "control elements" or "regulatory sequences" present in an expression vector are those non-translated regions of the vector-enhancers, promoters, 5' and 3' untranslated regions--which interact with host cellular proteins to carry out transcription and translation. Such elements may vary in their strength and specificity. Depending on the vector system and host utilized, any number of suitable transcription and translation elements, including constitutive and inducible promoters, may be used.

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For example, when cloning in bacterial systems, inducible promoters such as the hybrid lacZ promoter of the PBLUESCRIPT phagemid (Stratagene, La Jolla, Calif.) or PSPORT1 plasmid (Gibco BRL, Gaithersburg, MD) and the like may be used. In mammalian cell systems, promoters from mammalian genes or from mammalian viruses are generally preferred. If it is necessary to generate a cell line that contains multiple copies of the sequence encoding a polypeptide, vectors based on SV40 or EBV may be advantageously used with an appropriate selectable marker.

In bacterial systems, any of a number of expression vectors may be selected depending upon the use intended for the expressed polypeptide. For example, W. 259 - 30 when large quantities are needed, for example for the induction of antibodies, vectors which direct high level expression of fusion proteins that are readily purified may be used. Such vectors include, but are not limited to, the multifunctional E. coli cloning and expression vectors such as BLUESCRIPT (Stratagene), in which the sequence encoding the polypeptide of interest may be ligated into the vector in frame with sequences for the amino-terminal Met and the subsequent 7 residues of .beta.galactosidase so that a hybrid protein is produced; pIN vectors (Van Heeke, G. and S. M. Schuster (1989) J. Biol. Chem. 264:5503-5509); and the like, pGEX Vectors (Promega, Madison, Wis.) may also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption to glutathione-agarose beads followed by elution in the presence of free glutathione. Proteins made in such systems may be designed to include heparin, thrombin, or factor XA protease cleavage sites so that the cloned polypeptide of interest can be released from the GST moiety at will.

In the yeast, Saccharomyces cerevisiae, a number of vectors containing constitutive or inducible promoters such as alpha factor, alcohol oxidase, and PGH may be used. For reviews, see Ausubel et al. (supra) and Grant et al. (1987) Methods Enzymol. 153:516-544. 26 1/2021 1 1/2021 1 1/2021 1 1/2021 1 1/2021 1 1/2021 1 1/2021 1 1/2021 1 1/2021 1 1/2021

In cases where plant expression vectors are used, the expression of sequences encoding polypeptides may be driven by any of a number of promoters. For WO 01/51633 PCT/US01/01574

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example, viral promoters such as the 35S and 19S promoters of CaMV may be used alone or in combination with the omega leader sequence from TMV (Takamatsu, N. (1987) EMBO J. 6:307-311. Alternatively, plant promoters such as the small subunit of RUBISCO or heat shock promoters may be used (Coruzzi, G. et al. (1984) EMBO J. 3:1671-1680; Broglie, R. et al. (1984) Science 224:838-843; and Winter, J. et al. (1991) Results Probl. Cell Differ. 17:85-105). These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated transfection. Such techniques are described in a number of generally available reviews (see, for example, Hobbs, S. or Murry, L. E. in McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York, N.Y.; pp. 191-196).

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An insect system may also be used to express a polypeptide of interest. For example, in one such system, Autographa californica nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes in Spodoptera frugiperda cells or in Trichoplusia larvae. The sequences encoding the polypeptide may be cloned into a non-essential region of the virus, such as the polyhedrin gene, and placed under control of the polyhedrin promoter. Successful insertion of the polypeptide-encoding sequence will render the polyhedrin gene inactive and produce recombinant virus lacking coat protein. The recombinant viruses may then be used to infect, for example, S. frugiperda cells or Trichoplusia larvae in which the polypeptide of interest may be expressed (Engelhard, E. K. et al. (1994) *Proc. Natl. Acad. Sci. 91*:3224-3227).

In mammalian host cells, a number of viral-based expression systems are generally available. For example, in cases where an adenovirus is used as an expression vector, sequences encoding a polypeptide of interest may be ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a non-essential E1 or E3 region of the viral genome may be used to obtain a viable virus which is capable of expressing the polypeptide in infected host cells (Logan, J. and Shenk, T. (1984) *Proc. Natl. Acad. Sci. 81*:3655-3659). In addition, transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, may be used to increase expression in mammalian host cells.

Specific initiation signals may also be used to achieve more efficient translation of sequences encoding a polypeptide of interest. Such signals include the ATG initiation codon and adjacent sequences. In cases where sequences encoding the polypeptide, its initiation codon, and upstream sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control signals may be needed. However, in cases where only coding sequence, or a portion thereof, is inserted, exogenous translational control signals including the ATG initiation codon should be provided. Furthermore, the initiation codon should be in the correct reading frame to ensure translation of the entire insert. Exogenous translational elements and initiation codons may be of various origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of enhancers which are appropriate for the particular cell system which is used, such as those described in the literature (Scharf, D. et al. (1994) Results Probl. Cell Differ. 20:125-162).

In addition, a host cell strain may be chosen for its ability to modulate the expression of the inserted sequences or to process the expressed protein in the desired fashion. Such modifications of the polypeptide include, but are not limited to, acetylation, carboxylation. glycosylation, phosphorylation, lipidation, and acylation. Post-translational processing which cleaves a "prepro" form of the protein may also be used to facilitate correct insertion, folding and/or function. Different host cells such as CHO, COS, HeLa, MDCK, HEK293, and WI38, which have specific cellular machinery and characteristic mechanisms for such post-translational activities, may be chosen to ensure the correct modification and processing of the foreign protein.

For long-term, high-yield production of recombinant proteins, stable expression is generally preferred. For example, cell lines which stably express a polynucleotide of interest may be transformed using expression vectors which may contain viral origins of replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate vector. Following the introduction of the vector, cells may be allowed to grow for 1-2 days in an enriched media before they are switched to selective media. The purpose of the selectable marker is to confer resistance to selection, and its presence allows growth and recovery of cells which

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successfully express the introduced sequences. Resistant clones of stably transformed cells may be proliferated using tissue culture techniques appropriate to the cell type.

Any number of selection systems may be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase (Wigler, M. et al. (1977) Cell 11:223-32) and adenine phosphoribosyltransferase (Lowy, I. et al. (1990) Cell 22:817-23) genes which can be employed in tk.sup.- or aprt.sup.- cells, respectively. Also, antimetabolite, antibiotic or herbicide resistance can be used as the basis for selection; for example, dhfr which confers resistance to methotrexate (Wigler, M. et al. (1980) Proc. Natl. Acad. Sci. 77:3567-70); npt, which confers resistance to the aminoglycosides, neomycin and G-418 (Colbere-Garapin, F. et al (1981) J. Mol. Biol. 150:1-14); and als or pat, which confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively (Murry, supra). Additional selectable genes have been described, for example, trpB, which allows cells to utilize indole in place of tryptophan, or hisD, which allows cells to utilize histinol in place of histidine (Hartman, S. C. and R. C. Mulligan (1988) Proc. Natl. Acad. Sci. 85:8047-51). The use of visible markers has gained popularity with such markers as anthocyanins, beta-glucuronidase and its substrate GUS, and luciferase and its substrate luciferin, being widely used not only to identify transformants, but also to quantify the amount of transient or stable protein expression attributable to a specific vector system (Rhodes, C. A. et al. (1995) Methods Mol. Biol. 55:121-131).

Although the presence/absence of marker gene expression suggests that the gene of interest is also present, its presence and expression may need to be confirmed. For example, if the sequence encoding a polypeptide is inserted within a marker gene sequence, recombinant cells containing sequences can be identified by the absence of marker gene function. Alternatively, a marker gene can be placed in tandem with a polypeptide-encoding sequence under the control of a single promoter. Expression of the marker gene in response to induction or selection usually indicates expression of the tandem gene as well.

Alternatively, host cells that contain and express a desired polynucleotide sequence may be identified by a variety of procedures known to those of

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skill in the art. These procedures include, but are not limited to, DNA-DNA or DNA-RNA hybridizations and protein bioassay or immunoassay techniques which include, for example, membrane, solution, or chip based technologies for the detection and/or quantification of nucleic acid or protein.

A variety of protocols for detecting and measuring the expression of polynucleotide-encoded products, using either polyclonal or monoclonal antibodies specific for the product are known in the art. Examples include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), and fluorescence activated cell sorting (FACS). A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering epitopes on a given polypeptide may be preferred for some applications, but a competitive binding assay may also be employed. These and other assays are described, among other places, in Hampton, R. et al. (1990; Serological Methods, a Laboratory Manual, APS Press, St Paul. Minn.) and Maddox, D. E. et al. (1983; J. Exp. Med. 158:1211-1216).

A wide variety of labels and conjugation techniques are known by those skilled in the art and may be used in various nucleic acid and amino acid assays. Means for producing labeled hybridization or PCR probes for detecting sequences related to polynucleotides include oligolabeling, nick translation, end-labeling or PCR amplification using a labeled nucleotide. Alternatively, the sequences, or any portions thereof may be cloned into a vector for the production of an mRNA probe. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes in vitro by addition of an appropriate RNA polymerase such as T7, T3, or SP6 and labeled nucleotides. These procedures may be conducted using a variety of commercially available kits. Suitable reporter molecules or labels, which may be used include radionuclides, enzymes, fluorescent, chemiluminescent, or chromogenic agents as well as substrates, cofactors, inhibitors, magnetic particles, and the like.

Host cells transformed with a polynucleotide sequence of interest may be cultured under conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a recombinant cell may be secreted or contained intracellularly depending on the sequence and/or the vector used. As will be understood

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by those of skill in the art, expression vectors containing polynucleotides of the invention may be designed to contain signal sequences which direct secretion of the encoded polypeptide through a prokaryotic or eukaryotic cell membrane. Other recombinant constructions may be used to join sequences encoding a polypeptide of interest to nucleotide sequence encoding a polypeptide domain which will facilitate purification of soluble proteins. Such purification facilitating domains include, but are not limited to, metal chelating peptides such as histidine-tryptophan modules that allow purification on immobilized metals, protein A domains that allow purification on immobilized immunoglobulin, and the domain utilized in the FLAGS extension/affinity purification system (Immunex Corp., Seattle, Wash.). The inclusion of cleavable linker sequences such as those specific for Factor XA or enterokinase (Invitrogen. San Diego, Calif.) between the purification domain and the encoded polypeptide may be used to facilitate purification. One such expression vector provides for expression of a fusion protein containing a polypeptide of interest and a nucleic acid encoding 6 histidine residues preceding a thioredoxin or an enterokinase cleavage site. The histidine residues facilitate purification on IMIAC (immobilized metal ion affinity chromatography) as described in Porath, J. et al. (1992, Prot. Exp. Purif. 3:263-281) while the enterokinase cleavage site provides a means for purifying the desired polypeptide from the fusion protein. A discussion of vectors which contain fusion proteins is provided in Kroll, D. J. et al. (1993; DNA Cell Biol. 12:441-453).

In addition to recombinant production methods, polypeptides of the invention, and fragments thereof, may be produced by direct peptide synthesis using solid-phase techniques (Merrifield J. (1963) J. Am. Chem. Soc. 85:2149-2154). Protein synthesis may be performed using manual techniques or by automation. Automated synthesis may be achieved, for example, using Applied Biosystems 431A Peptide Synthesizer (Perkin Elmer). Alternatively, various fragments may be chemically synthesized separately and combined using chemical methods to produce the full length molecule.

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## Antibody Compositions, Fragments Thereof and Other Binding Agents

According to another aspect, the present invention further provides binding agents, such as antibodies and antigen-binding fragments thereof, that exhibit immunological binding to a tumor polypeptide disclosed herein, or to a portion, variant or derivative thereof. An antibody, or antigen-binding fragment thereof, is said to "specifically bind," "immunogically bind," and/or is "immunologically reactive" to a polypeptide of the invention if it reacts at a detectable level (within, for example, an ELISA assay) with the polypeptide, and does not react detectably with unrelated polypeptides under similar conditions.

Immunological binding, as used in this context, generally refers to the non-covalent interactions of the type which occur between an immunoglobulin molecule and an antigen for which the immunoglobulin is specific. The strength, or affinity of immunological binding interactions can be expressed in terms of the dissociation constant ( $K_d$ ) of the interaction, wherein a smaller  $K_d$  represents a greater affinity. Immunological binding properties of selected polypeptides can be quantified using methods well known in the art. One such method entails measuring the rates of antigen-binding site/antigen complex formation and dissociation, wherein those rates depend on the concentrations of the complex partners, the affinity of the interaction, and on geometric parameters that equally influence the rate in both directions. Thus, both the "on rate constant" ( $K_{on}$ ) and the "off rate constant" ( $K_{off}$ ) can be determined by calculation of the concentrations and the actual rates of association and dissociation. The ratio of  $K_{off}/K_{on}$  enables cancellation of all parameters not related to affinity, and is thus equal to the dissociation constant  $K_d$ . See, generally, Davies et al. (1990) Annual Rey. Biochem. 59:439-473.

An "antigen-binding site," or "binding portion" of an antibody refers to the part of the immunoglobulin molecule that participates in antigen binding. The antigen binding site is formed by amino acid residues of the N-terminal variable ("V") regions of the heavy ("H") and light ("L") chains. Three highly divergent stretches within the V regions of the heavy and light chains are referred to as "hypervariable regions" which are interposed between more conserved flanking stretches known as

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"framework regions," or "FRs". Thus the term "FR" refers to amino acid sequences which are naturally found between and adjacent to hypervariable regions in immunoglobulins. In an antibody molecule, the three hypervariable regions of a light chain and the three hypervariable regions of a heavy chain are disposed relative to each other in three dimensional space to form an antigen-binding surface. The antigen-binding surface is complementary to the three-dimensional surface of a bound antigen, and the three hypervariable regions of each of the heavy and light chains are referred to as "complementarity-determining regions," or "CDRs."

Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. For example, antibodies or other binding agents that bind to a tumor protein will preferably generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, more preferably at least about 30% of patients. Alternatively, or in addition, the antibody will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (e.g., blood, sera, sputum, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. Preferably, a statistically significant number of samples with and without the disease will be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent.

25 For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation

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of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, Eur. J. Immunol. 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (i.e., reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

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Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

A number of therapeutically useful molecules are known in the art which comprise antigen-binding sites that are capable of exhibiting immunological binding properties of an antibody molecule. The proteolytic enzyme papain preferentially cleaves IgG molecules to yield several fragments, two of which (the "F(ab)" fragments) each comprise a covalent heterodimer that includes an intact antigen-binding site. The enzyme pepsin is able to cleave IgG molecules to provide several fragments, including the "F(ab')<sub>2</sub> " fragment which comprises both antigen-binding sites. An "Fv" fragment can be produced by preferential proteolytic cleavage of an IgM, and on rare occasions IgG or IgA immunoglobulin molecule. Fv fragments are, however, more commonly derived using recombinant techniques known in the art. The Fv fragment includes a non-covalent V<sub>H</sub>::V<sub>L</sub> heterodimer including an antigen-binding site which retains much of the antigen recognition and binding capabilities of the native antibody molecule. Inbar et al. (1972) Proc. Nat. Acad. Sci. USA 69:2659-2662; Hochman et al. (1976) Biochem 15:2706-2710; and Ehrlich et al. (1980) Biochem 19:4091-4096.

A single chain Fv ("sFv") polypeptide is a covalently linked V<sub>H</sub>::V<sub>L</sub> heterodimer which is expressed from a gene fusion including V<sub>H</sub>- and V<sub>L</sub>-encoding genes linked by a peptide-encoding linker. Huston et al. (1988) Proc. Nat. Acad. Sci. USA 85(16):5879-5883. A number of methods have been described to discern chemical structures for converting the naturally aggregated—but chemically separated—light and heavy polypeptide chains from an antibody V region into an sFv molecule which will fold into a three dimensional structure substantially similar to the structure of an

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antigen-binding site. See, e.g., U.S. Pat. Nos. 5,091,513 and 5,132,405, to Huston et al.; and U.S. Pat. No. 4,946,778, to Ladner et al.

Each of the above-described molecules includes a heavy chain and a light chain CDR set, respectively interposed between a heavy chain and a light chain FR set which provide support to the CDRS and define the spatial relationship of the CDRs relative to each other. As used herein, the term "CDR set" refers to the three hypervariable regions of a heavy or light chain V region. Proceeding from the N-terminus of a heavy or light chain, these regions are denoted as "CDR1," "CDR2," and "CDR3" respectively. An antigen-binding site, therefore, includes six CDRs, comprising the CDR set from each of a heavy and a light chain V region. A polypeptide comprising a single CDR, (e.g., a CDR1, CDR2 or CDR3) is referred to herein as a "molecular recognition unit." Crystallographic analysis of a number of antigen-antibody complexes has demonstrated that the amino acid residues of CDRs form extensive contact with bound antigen, wherein the most extensive antigen contact is with the heavy chain CDR3. Thus, the molecular recognition units are primarily responsible for the specificity of an antigen-binding site.

As used herein, the term "FR set" refers to the four flanking amino acid sequences which frame the CDRs of a CDR set of a heavy or light chain V region. Some FR residues may contact bound antigen; however, FRs are primarily responsible for folding the V region into the antigen-binding site, particularly the FR residues directly adjacent to the CDRS. Within FRs, certain amino residues and certain structural features are very highly conserved. In this regard, all V region sequences contain an internal disulfide loop of around 90 amino acid residues. When the V regions fold into a binding-site, the CDRs are displayed as projecting loop motifs which form an antigen-binding surface. It is generally recognized that there are conserved structural regions of FRs which influence the folded shape of the CDR loops into certain "canonical" structures—regardless of the precise CDR amino acid sequence. Further, certain FR residues are known to participate in non-covalent interdomain contacts which stabilize the interaction of the antibody heavy and light chains.

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A number of "humanized" antibody molecules comprising an antigen-binding site derived from a non-human immunoglobulin have been described, including chimeric antibodies having rodent V regions and their associated CDRs fused to human constant domains (Winter et al. (1991) Nature 349:293-299; Lobuglio et al. (1989) Proc. Nat. Acad. Sci. USA 86:4220-4224; Shaw et al. (1987) J Immunol. 138:4534-4538; and Brown et al. (1987) Cancer Res. 47:3577-3583), rodent CDRs grafted into a human supporting FR prior to fusion with an appropriate human antibody constant domain (Riechmann et al. (1988) Nature 332:323-327; Verhoeyen et al. (1988) Science 239:1534-1536; and Jones et al. (1986) Nature 321:522-525), and rodent CDRs supported by recombinantly veneered rodent FRs (European Patent Publication No. 519,596, published Dec. 23, 1992). These "humanized" molecules are designed to minimize unwanted immunological response toward rodent antihuman antibody molecules which limits the duration and effectiveness of therapeutic applications of those moieties in human recipients.

As used herein, the terms "veneered FRs" and "recombinantly veneered FRs" refer to the selective replacement of FR residues from, e.g., a rodent heavy or light chain V region, with human FR residues in order to provide a xenogeneic molecule comprising an antigen-binding site which retains substantially all of the native FR polypeptide folding structure. Veneering techniques are based on the understanding that the ligand binding characteristics of an antigen-binding site are determined primarily by the structure and relative disposition of the heavy and light chain CDR sets within the antigen-binding surface. Davies et al. (1990) Ann. Rev. Biochem. 59:439-473. Thus, antigen binding specificity can be preserved in a humanized antibody only wherein the CDR structures, their interaction with each other, and their interaction with the rest of the V region domains are carefully maintained. By using veneering techniques, exterior (e.g., solvent-accessible) FR residues which are readily encountered by the immune system are selectively replaced with human residues to provide a hybrid molecule that comprises either a weakly immunogenic, or substantially non-immunogenic veneered surface.

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The process of veneering makes use of the available sequence data for human antibody variable domains compiled by Kabat et al., in Sequences of Proteins of Immunological Interest, 4th ed., (U.S. Dept. of Health and Human Services, U.S. Government Printing Office, 1987), updates to the Kabat database, and other accessible U.S. and foreign databases (both nucleic acid and protein). Solvent accessibilities of V region amino acids can be deduced from the known three-dimensional structure for human and murine antibody fragments. There are two general steps in veneering a murine antigen-binding site. Initially, the FRs of the variable domains of an antibody molecule of interest are compared with corresponding FR sequences of human variable domains obtained from the above-identified sources. The most homologous human V regions are then compared residue by residue to corresponding murine amino acids. The residues in the murine FR which differ from the human counterpart are replaced by the residues present in the human moiety using recombinant techniques well known in the art. Residue switching is only carried out with moieties which are at least partially exposed (solvent accessible), and care is exercised in the replacement of amino acid residues which may have a significant effect on the tertiary structure of V region domains, such as proline, glycine and charged amino acids.

In this manner, the resultant "veneered" murine antigen-binding sites are thus designed to retain the murine CDR residues, the residues substantially adjacent to the CDRs, the residues identified as buried or mostly buried (solvent inaccessible), the residues believed to participate in non-covalent (e.g., electrostatic and hydrophobic) contacts between heavy and light chain domains, and the residues from conserved structural regions of the FRs which are believed to influence the "canonical" tertiary structures of the CDR loops. These design criteria are then used to prepare recombinant nucleotide sequences which combine the CDRs of both the heavy and light chain of a murine antigen-binding site into human-appearing FRs that can be used to transfect mammalian cells for the expression of recombinant human antibodies which exhibit the antigen specificity of the murine antibody molecule.

In another embodiment of the invention, monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in

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this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include <sup>90</sup>Y, <sup>123</sup>I, <sup>125</sup>I, <sup>131</sup>I, <sup>186</sup>Re, <sup>188</sup>Re, <sup>211</sup>At, and <sup>212</sup>Bi. Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diptheria toxin, cholera toxin, gelonin, Pseudomonas exotoxin, Shigella toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (e.g., covalently bonded) to a suitable monoclonal antibody either directly or indirectly (e.g., via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (e.g., a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, e.g., U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the

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intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (e.g., U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (e.g., U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (e.g., U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (e.g., U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (e.g., U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers that provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (e.g., U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (e.g., U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (e.g., U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

## T Cell Compositions

The present invention, in another aspect, provides T cells specific for a tumor polypeptide disclosed herein, or for a variant or derivative thereof. Such cells

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may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the Isolex<sup>™</sup> System, available from Nexell Therapeutics, Inc. (Irvine, CA; see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a polypeptide, polynucleotide encoding a polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide of interest. Preferably, a tumor polypeptide or polynucleotide of the invention is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a polypeptide of the present invention if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., Cancer Res. 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days will typically result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-y) is indicative of T cell activation (see Coligan et E-135

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al., Current Protocols in Immunology, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4<sup>+</sup> and/or CD8<sup>+</sup>. Tumor polypeptide-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from a patient, a related donor or an unrelated donor, and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4<sup>+</sup> or CD8<sup>+</sup> T cells that proliferate in response to a tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of the tumor polypeptide can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

## Pharmaceutical Compositions

In additional embodiments, the present invention concerns formulation of one or more of the polynucleotide, polypeptide, T-cell and/or antibody compositions disclosed herein in pharmaceutically-acceptable carriers for administration to a cell or an animal, either alone, or in combination with one or more other modalities of therapy.

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It will be understood that, if desired, a composition as disclosed herein may be administered in combination with other agents as well, such as, e.g., other proteins or polypeptides or various pharmaceutically-active agents. In fact, there is virtually no limit to other components that may also be included, given that the additional agents do not cause a significant adverse effect upon contact with the target cells or host tissues. The compositions may thus be delivered along with various other agents as required in the particular instance. Such compositions may be purified from host cells or other biological sources, or alternatively may be chemically synthesized as

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described herein. Likewise, such compositions may further comprise substituted or derivatized RNA or DNA compositions.

Therefore, in another aspect of the present invention, pharmaceutical compositions are provided comprising one or more of the polynucleotide, polypeptide, antibody, and/or T-cell compositions described herein in combination with a physiologically acceptable carrier. In certain preferred embodiments, the pharmaceutical compositions of the invention comprise immunogenic polynucleotide and/or polypeptide compositions of the invention for use in prophylactic and theraputic vaccine applications. Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Generally, such compositions will comprise one or more polynucleotide and/or polypeptide compositions of the present invention in combination with one or more immunostimulants.

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It will be apparent that any of the pharmaceutical compositions described herein can contain pharmaceutically acceptable salts of the polynucleotides and polypeptides of the invention. Such salts can be prepared, for example, from pharmaceutically acceptable non-toxic bases, including organic bases (e.g., salts of primary, secondary and tertiary amines and basic amino acids) and inorganic bases (e.g., sodium, potassium, lithium, ammonium, calcium and magnesium salts).

In another embodiment, illustrative immunogenic compositions, e.g., vaccine compositions, of the present invention comprise DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated in situ. As noted above, the polynucleotide may be administered within any of a variety of delivery systems known to those of ordinary skill in the art. Indeed, numerous gene delivery techniques are well known in the art, such as those described by Rolland, Crit. Rev. Therap. Drug Carrier Systems 15:143-198, 1998, and references cited therein. Appropriate polynucleotide expression systems will, of course, contain the necessary regulatory DNA regulatory sequences for expression in a patient (such as a suitable promoter and terminating signal). Alternatively, bacterial delivery systems may involve

the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope.

Therefore, in certain embodiments, polynucleotides encoding immunogenic polypeptides described herein are introduced into suitable mammalian host cells for expression using any of a number of known viral-based systems. In one illustrative embodiment, retroviruses provide a convenient and effective platform for gene delivery systems. A selected nucleotide sequence encoding a polypeptide of the present invention can be inserted into a vector and packaged in retroviral particles using techniques known in the art. The recombinant virus can then be isolated and delivered to a subject. A number of illustrative retroviral systems have been described (e.g., U.S. Pat. No. 5,219,740; Miller and Rosman (1989) BioTechniques 7:980-990; Miller, A. D. (1990) Human Gene Therapy 1:5-14; Scarpa et al. (1991) Virology 180:849-852; Burns et al. (1993) Proc. Natl. Acad. Sci. USA 90:8033-8037; and Boris-Lawrie and Temin (1993) Cur. Opin. Genet. Develop. 3:102-109.

In addition, a number of illustrative adenovirus-based systems have also been described. Unlike retroviruses which integrate into the host genome, adenoviruses persist extrachromosomally thus minimizing the risks associated with insertional mutagenesis (Haj-Ahmad and Graham (1986) J. Virol. 57:267-274; Bett et al. (1993) J. Virol. 67:5911-5921; Mittereder et al. (1994) Human Gene Therapy 5:717-729; Seth et al. (1994) J. Virol. 68:933-940; Barr et al. (1994) Gene Therapy 1:51-58; Berkner, K. L. (1988) BioTechniques 6:616-629; and Rich et al. (1993) Human Gene Therapy 4:461-476).

Various adeno-associated virus (AAV) vector systems have also been developed for polynucleotide delivery. AAV vectors can be readily constructed using techniques well known in the art. See, e.g., U.S. Pat. Nos. 5,173,414 and 5,139,941; International Publication Nos. WO 92/01070 and WO 93/03769; Lebkowski et al. (1988) Molec. Cell. Biol. 8:3988-3996; Vincent et al. (1990) Vaccines 90 (Cold Spring Harbor Laboratory Press); Carter, B. J. (1992) Current Opinion in Biotechnology 3:533-539; Muzyczka, N. (1992) Current Topics in Microbiol. and Immunol. 158:97-129;

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Kotin, R. M. (1994) Human Gene Therapy 5:793-801; Shelling and Smith (1994) Gene Therapy 1:165-169; and Zhou et al. (1994) J. Exp. Med. 179:1867-1875.

Additional viral vectors useful for delivering the polynucleotides encoding polypeptides of the present invention by gene transfer include those derived from the pox family of viruses, such as vaccinia virus and avian poxvirus. By way of example, vaccinia virus recombinants expressing the novel molecules can be constructed as follows. The DNA encoding a polypeptide is first inserted into an appropriate vector so that it is adjacent to a vaccinia promoter and flanking vaccinia DNA sequences, such as the sequence encoding thymidine kinase (TK). This vector is then used to transfect cells which are simultaneously infected with vaccinia. Homologous recombination serves to insert the vaccinia promoter plus the gene encoding the polypeptide of interest into the viral genome. The resulting TK.sup.(-) recombinant can be selected by culturing the cells in the presence of 5-bromodeoxyuridine and picking viral plaques resistant thereto.

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A vaccinia-based infection/transfection system can be conveniently used to provide for inducible, transient expression or coexpression of one or more polypeptides described herein in host cells of an organism. In this particular system, cells are first infected in vitro with a vaccinia virus recombinant that encodes the bacteriophage T7 RNA polymerase. This polymerase displays exquisite specificity in that it only transcribes templates bearing T7 promoters. Following infection, cells are transfected with the polynucleotide or polynucleotides of interest, driven by a T7 promoter. The polymerase expressed in the cytoplasm from the vaccinia virus recombinant transcribes the transfected DNA into RNA which is then translated into polypeptide by the host translational machinery. The method provides for high level, transient, cytoplasmic production of large quantities of RNA and its translation products. See, e.g., Elroy-Stein and Moss, Proc. Natl. Acad. Sci. USA (1990) 87:6743-6747; Fuerst et al. Proc. Natl. Acad. Sci. USA (1986) 83:8122-8126.

Alternatively, avipoxviruses, such as the fowlpox and canarypox viruses, can also be used to deliver the coding sequences of interest. Recombinant avipox viruses, expressing immunogens from mammalian pathogens, are known to confer

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protective immunity when administered to non-avian species. The use of an Avipox vector is particularly desirable in human and other mammalian species since members of the Avipox genus can only productively replicate in susceptible avian species and therefore are not infective in mammalian cells. Methods for producing recombinant Avipoxviruses are known in the art and employ genetic recombination, as described above with respect to the production of vaccinia viruses. See, e.g., WO 91/12882; WO 89/03429; and WO 92/03545.

Any of a number of alphavirus vectors can also be used for delivery of polynucleotide compositions of the present invention, such as those vectors described in U.S. Patent Nos. 5,843,723; 6,015,686; 6,008,035 and 6,015,694. Certain vectors based on Venezuelan Equine Encephalitis (VEE) can also be used, illustrative examples of which can be found in U.S. Patent Nos. 5,505,947 and 5,643,576.

Moreover, molecular conjugate vectors, such as the adenovirus chimeric vectors described in Michael et al. J. Biol. Chem. (1993) 268:6866-6869 and Wagner et al. Proc. Natl. Acad. Sci. USA (1992) 89:6099-6103, can also be used for gene delivery under the invention.

Additional illustrative information on these and other known viral-based delivery systems can be found, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA 86*:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci. 569*:86-103, 1989; Flexner et al., *Vaccine 8*:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques 6*:616-627, 1988; Rosenfeld et al., *Science 252*:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA 91*:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA 90*:11498-11502, 1993; Guzman et al., *Circulation 88*:2838-2848, 1993; and Guzman et al., *Cir. Res. 73*:1202-1207, 1993.

In certain embodiments, a polynucleotide may be integrated into the genome of a target cell. This integration may be in a specific location and orientation via homologous recombination (gene replacement) or it may be integrated in a random, non-specific location (gene augmentation). In yet further embodiments, the polynucleotide may be stably maintained in the cell as a separate, episomal segment of

DNA. Such polynucleotide segments or "episomes" encode sequences sufficient to permit maintenance and replication independent of or in synchronization with the host cell cycle. The manner in which the expression construct is delivered to a cell and where in the cell the polynucleotide remains is dependent on the type of expression construct employed.

In another embodiment of the invention, a polynucleotide is administered/delivered as "naked" DNA, for example as described in Ulmer et al., Soience 259:1745-1749, 1993 and reviewed by Cohen, Science 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

In still another embodiment, a composition of the present invention can be delivered via a particle bombardment approach, many of which have been described. In one illustrative example, gas-driven particle acceleration can be achieved with devices such as those manufactured by Powderject Pharmaceuticals PLC (Oxford, UK) and Powderject Vaccines Inc. (Madison, WI), some examples of which are described in U.S. Patent Nos. 5,846,796; 6,010,478; 5,865,796; 5,584,807; and EP Patent No. 0500 799. This approach offers a needle-free delivery approach wherein a dry powder formulation of microscopic particles, such as polynucleotide or polypeptide particles, are accelerated to high speed within a helium gas jet generated by a hand held device, propelling the particles into a target tissue of interest.

In a related embodiment, other devices and methods that may be useful for gas-driven needle-less injection of compositions of the present invention include those provided by Bioject, Inc. (Portland, OR), some examples of which are described in U.S. Patent Nos. 4,790,824; 5,064,413; 5,312,335; 5,383,851; 5,399,163; 5,520,639 and 5,993,412.

According to another embodiment, the pharmaceutical compositions described herein will comprise one or more immunostimulants in addition to the immunogenic polynucleotide, polypeptide, antibody, T-cell and/or APC compositions of this invention. An immunostimulant refers to essentially any substance that enhances or potentiates an immune response (antibody and/or cell-mediated) to an exogenous

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antigen. One preferred type of immunostimulant comprises an adjuvant. adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, Bortadella pertussis or Mycobacterium tuberculosis derived proteins. Certain adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF, interleukin-2, -7, -12, and other like growth factors, may also be used as etracia adjuvants. Pro ekit ke feroe ik hogo a en herg jaligeren e etroppe e eo

Within certain embodiments of the invention, the adjuvant composition 15 is preferably one that induces an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN-y, TNFa, IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-20 type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, Ann. Rev. Immunol. 7:145-173, 1989.

Certain preferred adjuvants for eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3de-O-acylated monophosphoryl lipid A, together with an aluminum salt. adjuvants are available from Corixa Corporation (Seattle, WA; see, for example, US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing

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oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555, WO 99/33488 and U.S. Patent Nos. 6,008,200 and 5,856,462. Immunostimulatory DNA sequences are also described, for example, by Sato et al., Science 273:352, 1996. Another preferred adjuvant comprises a saponin, such as Quil A, or derivatives thereof, including QS21 and QS7 (Aquila Biopharmaceuticals Inc., Framingham, MA); Escin; Digitonin; or Gypsophila or Cħenopodium quinoa saponins. Other preferred formulations include more than one saponin in the adjuvant combinations of the present invention, for example combinations of at least two of the following group comprising QS21, QS7, Quil A, β-escin, or digitonin.

Alternatively the saponin formulations may be combined with vaccine vehicles composed of chitosan or other polycationic polymers, polylactide and polylactide-co-glycolide particles, poly-N-acetyl glucosamine-based polymer matrix, particles composed of polysaccharides or chemically modified polysaccharides, liposomes and lipid-based particles, particles composed of glycerol monoesters, etc. The saponins may also be formulated in the presence of cholesterol to form particulate structures such as liposomes or ISCOMs. Furthermore, the saponins may be formulated together with a polyoxyethylene ether or ester, in either a non-particulate solution or suspension, or in a particulate structure such as a paucilamelar liposome or ISCOM. The saponins may also be formulated with excipients such as Carbopol<sup>R</sup> to increase viscosity, or may be formulated in a dry powder form with a powder excipient such as lactose.

In one preferred embodiment, the adjuvant system includes the combination of a monophosphoryl lipid A and a saponin derivative, such as the combination of QS21 and 3D-MPL® adjuvant, as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprise an oil-in-water emulsion and tocopherol. Another particularly preferred adjuvant formulation employing QS21, 3D-

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MPL® adjuvant and tocopherol in an oil-in-water emulsion is described in WO 95/17210.

Another enhanced adjuvant system involves the combination of a CpG-containing oligonucleotide and a saponin derivative particularly the combination of CpG and QS21 is disclosed in WO 00/09159. Preferably the formulation additionally comprises an oil in water emulsion and tocopherol.

Additional illustrative adjuvants for use in the pharmaceutical compositions of the invention include Montanide ISA 720 (Seppic, France), SAF (Chiron, California, United States), ISCOMS (CSL), MF-59 (Chiron), the SBAS series of adjuvants (e.g., SBAS-2 or SBAS-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (Enhanzyn<sup>®</sup>; Corixa, Hamilton, MT), RC-529 (Corixa, Hamilton, MT) and other aminoalkyl glucosaminide 4-phosphates (AGPs), such as those described in pending U.S. Patent Application Serial Nos. 08/853,826 and 09/074,720, the disclosures of which are incorporated herein by reference in their entireties, and polyoxyethylene ether adjuvants such as those described in WO 99/52549A1.

Other preferred adjuvants include adjuvant molecules of the general formula

(I):  $HO(CH_2CH_2O)_n$ -A-R,

wherein, n is 1-50, A is a bond or -C(O)-, R is  $C_{1-50}$  alkyl or Phenyl  $C_{1-50}$  alkyl.

One embodiment of the present invention consists of a vaccine formulation comprising a polyoxyethylene ether of general formula (I), wherein n is between 1 and 50, preferably 4-24, most preferably 9; the R component is C<sub>1-50</sub>, preferably C<sub>4</sub>-C<sub>20</sub> alkyl and most preferably C<sub>12</sub> alkyl, and A is a bond. The concentration of the polyoxyethylene ethers should be in the range 0.1-20%, preferably from 0.1-10%, and most preferably in the range 0.1-1%. Preferred polyoxyethylene ethers are selected from the following group: polyoxyethylene-9-lauryl ether, polyoxyethylene-9-steoryl ether, polyoxyethylene-8-steoryl ether, polyoxyethylene-4-lauryl ether, polyoxyethylene-35-lauryl ether, and polyoxyethylene-23-lauryl ether. Polyoxyethylene ethers such as polyoxyethylene lauryl ether are described in the Merck index (12<sup>th</sup> edition: entry 7717). These adjuvant molecules are described in WO

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99/52549. The polyoxyethylene ether according to the general formula (I) above may, if desired, be combined with another adjuvant. For example, a preferred adjuvant combination is preferably with CpG as described in the pending UK patent application GB 9820956.2.

According to another embodiment of this invention, an immunogenic composition described herein is delivered to a host via antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects per se and/or to be immunologically compatible with the receiver (i.e., matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, Nature 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (see Timmerman and Levy, Ann. Rev. Med. 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate in situ, with marked cytoplasmic processes (dendrites) visible in vitro), their ability to take up, process and present antigens with high efficiency and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells in vivo or ex vivo, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (see Zitvogel et al., Nature Med. 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, 30 bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph , **5** 

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nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNFα to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNFα, CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fcy receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (e.g., CD54 and CD11) and costimulatory molecules (e.g., CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide of the invention (or portion or other variant thereof) such that the encoded polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place ex vivo, and a pharmaceutical composition comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs in vivo. In vivo and ex vivo transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., Immunology and cell Biology 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the tumor polypeptide, DNA (naked or within a plasmid vector) or

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RNA; or with antigen-expressing recombinant bacterium or viruses (e.g., vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (e.g., a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will typically vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, mucosal, intravenous, intracranial, intraperitoneal, subcutaneous and intramuscular administration.

Carriers for use within such pharmaceutical compositions biocompatible, and may also be biodegradable. In certain embodiments, the formulation preferably provides a relatively constant level of active component release. In other embodiments, however, a more rapid rate of release immediately upon administration may be desired. The formulation of such compositions is well within the level of ordinary skill in the art using known techniques. Illustrative carriers useful in this regard include microparticles of poly(lactide-co-glycolide), polyacrylate, latex, starch, cellulose, dextran and the like. Other illustrative delayed-release carriers include supramolecular biovectors, which comprise a non-liquid hydrophilic core (e.g., a cross-linked polysaccharide or oligosaccharide) and, optionally, an external layer comprising an amphiphilic compound, such as a phospholipid (see e.g., U.S. Patent No. 5,151,254 and PCT applications WO 94/20078, WO/94/23701 and WO 96/06638). The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

In another illustrative embodiment, biodegradable microspheres (e.g., polylactate polyglycolate) are employed as carriers for the compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268; 5,075,109; 5,928,647; 5,811,128; 5,820,883; 5,853,763;

5,814,344, 5,407,609 and 5,942,252. Modified hepatitis B core protein carrier systems. such as described in WO/99 40934, and references cited therein, will also be useful for many applications. Another illustrative carrier/delivery system employs a carrier comprising particulate-protein complexes, such as those described in U.S. Patent No. 5,928,647, which are capable of inducing a class I-restricted cytotoxic T lymphocyte responses in a host.

The pharmaceutical compositions of the invention will often further comprise one or more buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, bacteriostats, chelating agents such as EDTA or glutathione, adjuvants (e.g., aluminum hydroxide), solutes that render the formulation isotonic, hypotonic or weakly hypertonic with the blood of a recipient, suspending agents, thickening agents and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate.

The pharmaceutical compositions described herein may be presented in unit-dose or multi-dose containers, such as sealed ampoules or vials. Such containers are typically sealed in such a way to preserve the sterility and stability of the formulation until use. In general, formulations may be stored as suspensions, solutions or emulsions in oily or aqueous vehicles. Alternatively, a pharmaceutical composition may be stored in a freeze-dried condition requiring only the addition of a sterile liquid carrier immediately prior to use.

The development of suitable dosing and treatment regimens for using the particular compositions described herein in a variety of treatment regimens, including e.g., oral, parenteral, intravenous, intranasal, and intramuscular administration and formulation, is well known in the art, some of which are briefly discussed below for general purposes of illustration.

may be delivered via oral administration to an animal. As such, these compositions may be formulated with an inert diluent or with an assimilable edible carrier, or they

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may be enclosed in hard- or soft-shell gelatin capsule, or they may be compressed into tablets, or they may be incorporated directly with the food of the diet.

The active compounds may even be incorporated with excipients and used in the form of ingestible tablets, buccal tables, troches, capsules, elixirs, suspensions, syrups, wafers, and the like (see, for example, Mathiowitz et al., Nature 1997 Mar 27;386(6623):410-4; Hwang et al., Crit Rev Ther Drug Carrier Syst 1998;15(3):243-84; U. S. Patent 5,641,515; U. S. Patent 5,580,579 and U. S. Patent 5,792,451). Tablets, troches, pills, capsules and the like may also contain any of a variety of additional components, for example, a binder, such as gum tragacanth, acacia, 10 cornstarch, or gelatin; excipients, such as dicalcium phosphate; a disintegrating agent, such as corn starch, potato starch, alginic acid and the like; a lubricant, such as magnesium stearate; and a sweetening agent, such as sucrose, lactose or saccharin may be added or a flavoring agent, such as peppermint, oil of wintergreen, or cherry flavoring. When the dosage unit form is a capsule, it may contain, in addition to materials of the above type, a liquid carrier. Various other materials may be present as coatings or to otherwise modify the physical form of the dosage unit. For instance, tablets, pills, or capsules may be coated with shellac, sugar, or both. Of course, any material used in preparing any dosage unit form should be pharmaceutically pure and substantially non-toxic in the amounts employed. In addition, the active compounds may be incorporated into sustained-release preparation and formulations.

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Typically, these formulations will contain at least about 0.1% of the active compound or more, although the percentage of the active ingredient(s) may, of course, be varied and may conveniently be between about 1 or 2% and about 60% or 70% or more of the weight or volume of the total formulation. Naturally, the amount of active compound(s) in each therapeutically useful composition may be prepared is such a way that a suitable dosage will be obtained in any given unit dose of the compound. Factors such as solubility, bioavailability, biological half-life, route of administration, product shelf life, as well as other pharmacological considerations will be contemplated by one skilled in the art of preparing such pharmaceutical formulations, and as such, a variety of dosages and treatment regimens may be desirable.

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For oral administration, the compositions of the present invention may alternatively be incorporated with one or more excipients in the form of a mouthwash, dentifrice, buccal tablet, oral spray, or sublingual orally-administered formulation. Alternatively, the active ingredient may be incorporated into an oral solution such as one containing sodium borate, glycerin and potassium bicarbonate, or dispersed in a dentifrice, or added in a therapeutically-effective amount to a composition that may include water, binders, abrasives, flavoring agents, foaming agents, and humectants. Alternatively the compositions may be fashioned into a tablet or solution form that may be placed under the tongue or otherwise dissolved in the mouth.

In certain circumstances it will be desirable to deliver the pharmaceutical compositions disclosed herein parenterally, intravenously, intramuscularly, or even intraperitoneally. Such approaches are well known to the skilled artisan, some of which are further described, for example, in U. S. Patent 5,543,158; U. S. Patent 5,641,515 and U. S. Patent 5,399,363. In certain embodiments, solutions of the active compounds as free base or pharmacologically acceptable salts may be prepared in water suitably mixed with a surfactant, such as hydroxypropylcellulose. Dispersions may also be prepared in glycerol, liquid polyethylene glycols, and mixtures thereof and in oils. Under ordinary conditions of storage and use, these preparations generally will contain a preservative to prevent the growth of microorganisms.

Illustrative pharmaceutical forms suitable for injectable use include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions (for example, see U. S. Patent 5,466,468). In all cases the form must be sterile and must be fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms, such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (e.g., glycerol, propylene glycol, and liquid polyethylene glycol, and the like), suitable mixtures thereof, and/or vegetable oils. Proper fluidity may be maintained, for example, by the use of a coating, such as lecithin, by the maintenance of the required particle size in the case of dispersion and/or

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by the use of surfactants. The prevention of the action of microorganisms can be facilitated by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars or sodium chloride. Prolonged absorption of the injectable compositions can be brought about by the use in the compositions of agents delaying absorption, for example, aluminum monostearate and gelatin.

In one embodiment, for parenteral administration in an aqueous solution, the solution should be suitably buffered if necessary and the liquid diluent first rendered isotonic with sufficient saline or glucose. These particular aqueous solutions are especially suitable for intravenous, intramuscular, subcutaneous and intraperitoneal administration. In this connection, a sterile aqueous medium that can be employed will be known to those of skill in the art in light of the present disclosure. For example, one dosage may be dissolved in 1 ml of isotonic NaCl solution and either added to 1000 ml of hypodermoclysis fluid or injected at the proposed site of infusion, (see for example, "Remington's Pharmaceutical Sciences" 15th Edition, pages 1035-1038 and 1570-1580). Some variation in dosage will necessarily occur depending on the condition of the subject being treated. Moreover, for human administration, preparations will of course preferably meet sterility, pyrogenicity, and the general safety and purity standards as required by FDA Office of Biologics standards.

In another embodiment of the invention, the compositions disclosed herein may be formulated in a neutral or salt form. Illustrative pharmaceutically-acceptable salts include the acid addition salts (formed with the free amino groups of the protein) and which are formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, or such organic acids as acetic, oxalic, tartaric, mandelic, and the like. Salts formed with the free carboxyl groups can also be derived from inorganic bases such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic bases as isopropylamine, trimethylamine, histidine, procaine and the like. Upon formulation, solutions will be

administered in a manner compatible with the dosage formulation and in such amount as is therapeutically effective.

The carriers can further comprise any and all solvents, dispersion media, vehicles, coatings, diluents, antibacterial and antifungal agents, isotonic and absorption delaying agents, buffers, carrier solutions, suspensions, colloids, and the like. The use of such media and agents for pharmaceutical active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active ingredient, its use in the therapeutic compositions is contemplated. Supplementary active ingredients can also be incorporated into the compositions. The phrase "pharmaceutically-acceptable" refers to molecular entities and compositions that do not produce an allergic or similar untoward reaction when administered to a human.

In certain embodiments, the pharmaceutical compositions may be delivered by intranasal sprays, inhalation, and/or other aerosol delivery vehicles. Methods for delivering genes, nucleic acids, and peptide compositions directly to the lungs via nasal aerosol sprays has been described, e.g., in U. S. Patent 5,756,353 and U. S. Patent 5,804,212. Likewise, the delivery of drugs using intranasal microparticle resins (Takenaga et al., J Controlled Release 1998 Mar 2;52(1-2):81-7) and lysophosphatidyl-glycerol compounds (U. S. Patent 5,725,871) are also well-known in the pharmaceutical arts. Likewise, illustrative transmucosal drug delivery in the form of a polytetrafluoroetheylene support matrix is described in U. S. Patent 5,780,045.

In certain embodiments, liposomes, nanocapsules, microparticles, lipid particles, vesicles, and the like, are used for the introduction of the compositions of the present invention into suitable host cells/organisms. In particular, the compositions of the present invention may be formulated for delivery either encapsulated in a lipid particle, a liposome, a vesicle, a nanosphere, or a nanoparticle or the like. Alternatively, compositions of the present invention can be bound, either covalently or non-covalently, to the surface of such carrier vehicles.

The formation and use of liposome and liposome-like preparations as potential drug carriers is generally known to those of skill in the art (see for example, Lasic, Trends Biotechnol 1998 Jul;16(7):307-21; Takakura, Nippon Rinsho 1998

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Mar;56(3):691-5; Chandran et al., Indian J Exp Biol. 1997 Aug;35(8):801-9; Margalit, Crit Rev Ther Drug Carrier Syst. 1995;12(2-3):233-61; U.S. Patent 5,567,434; U.S. Patent 5,552,157; U.S. Patent 5,565,213; U.S. Patent 5,738,868 and U.S. Patent 5,795,587, each specifically incorporated herein by reference in its entirety).

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Liposomes have been used successfully with a number of cell types that are normally difficult to transfect by other procedures, including T cell suspensions, primary hepatocyte cultures and PC 12 cells (Renneisen et al., J Biol Chem. 1990 Sep 25;265(27):16337-42; Muller et al., DNA Cell Biol. 1990 Apr;9(3):221-9). In addition, liposomes are free of the DNA length constraints that are typical of viral-based delivery systems. Liposomes have been used effectively to introduce genes, various drugs, radiotherapeutic agents, enzymes, viruses, transcription factors, allosteric effectors and the like, into a variety of cultured cell lines and animals. Furthermore, he use of liposomes does not appear to be associated with autoimmune responses or unacceptable toxicity after systemic delivery.

In certain embodiments, liposomes are formed from phospholipids that are dispersed in an aqueous medium and spontaneously form multilamellar concentric bilayer vesicles (also termed multilamellar vesicles (MLVs).

Alternatively, in other embodiments, the invention provides for pharmaceutically-acceptable nanocapsule formulations of the compositions of the present invention. Nanocapsules can generally entrap compounds in a stable and reproducible way (see, for example, Quintanar-Guerrero et al., Drug Dev Ind Pharm. 1998 Dec;24(12):1113-28). To avoid side effects due to intracellular polymeric overloading, such ultrafine particles (sized around 0.1 µm) may be designed using polymers able to be degraded in vivo. Such particles can be made as described, for example, by Couvreur et al., Crit Rev Ther Drug Carrier Syst. 1988;5(1):1-20; zur Muhlen et al., Eur J Pharm Biopharm. 1998 Mar;45(2):149-55; Zambaux et al. J Controlled Release. 1998 Jan 2;50(1-3):31-40; and U. S. Patent 5,145,684.

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## **Cancer Therapeutic Methods**

In further aspects of the present invention, the pharmaceutical compositions described herein may be used for the treatment of cancer, particularly for the immunotherapy of prostate cancer. Within such methods, the pharmaceutical compositions described herein are administered to a patient, typically a warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs. As discussed above, administration of the pharmaceutical compositions may be by any suitable method, including administration by intravenous, intraperitoneal, intramuscular, subcutaneous, intranasal, intradermal, anal, vaginal, topical and oral routes.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides as provided herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8<sup>+</sup> cytotoxic T lymphocytes and CD4<sup>+</sup> T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The

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polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth in vitro, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition in vivo are well known in the art. Such in vitro culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast and/or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term in vivo. Studies have shown that cultured effector cells can be induced to grow in vivo and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (see, for example, Cheever et al., Immunological Reviews 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated ex vivo for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions described herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (e.g., intracutaneous,

intramuscular, intravenous or subcutaneous), intranasally (e.g., by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (i.e., untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccinedependent generation of cytolytic effector cells capable of killing the patient's tumor 10 cells in vitro. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (e.g., more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to nonvaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose 15 ranges from about 25 μg to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical 20 outcome (e.g., more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. preexisting immune responses to a tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

## Cancer Detection and Diagnostic Compositions, Methods and Kits

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In general, a cancer may be detected in a patient based on the presence of one or more prostate tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, sputum urine and/or tumor biopsies)

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obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., 10 Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) 15 comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length prostate tumor proteins and polypeptide portions thereof to which the binding agent binds, as 30 described above. And the second of the second

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The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 μg, and preferably about 100 ng to about 1 μg, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (see, e.g., Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay.

30 This assay may be performed by first contacting an antibody that has been immobilized

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on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

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More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20<sup>TM</sup> (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (i.e., incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20<sup>TM</sup>. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibodypolypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., Clinical Epidemiology: A Basic Science for Clinical Medicine, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (i.e., sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (i.e., the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

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In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1µg, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

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Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use tumor polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such tumor protein specific antibodies may correlate with the presence of a cancer.

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A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient is incubated with a tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated in vitro for 2-9 days (typically 4 days) at 37°C with polypeptide (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of tumor polypeptide to serve as a control. For CD4<sup>+</sup> T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8+ T cells. activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a tumor protein of the invention that is at least 10

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nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes hybridize to a polynucleotide encoding a polypeptide described herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence as disclosed herein. Techniques for both PCR based assays and hybridization assays are well known in the art (see, for example, Mullis et al., Cold Spring Harbor Symp. Quant. Biol., 51:263, 1987; Erlich ed., PCR Technology, Stockton Press, NY, 1989).

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One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the compositions described herein may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide(s) evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the

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cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple tumor protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided herein may be combined with assays for other known tumor antigens.

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a tumor protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a tumor protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a tumor protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be

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present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a tumor protein.

The following Examples are offered by way of illustration and not by way of limitation.

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#### <u>EXAMPLES</u>

#### **EXAMPLE 1**

## ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES

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This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from prostate tumor poly A<sup>+</sup> RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol. Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A<sup>+</sup> RNA was then purified using a Qiagen oligotex spin column mRNA purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-strand cDNA was synthesized using the Notl/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with Notl. Following size fractionation with Chroma Spin-1000 columns (Clontech, Palo Alto, CA), the cDNA was ligated into the EcoRI/Notl site of pCDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was prepared from a pool of six tissue specimens (Clontech). The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis.

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The prostate tumor library contained 1.64 x 10<sup>7</sup> independent colonies, with 70% of clones having an insert and the average insert size being 1745 base pairs. The normal pancreas cDNA library contained 3.3 x 106 independent colonies, with 69% of clones having inserts and the average insert size being 1120 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

cDNA library subtraction was performed using the above prostate tumor and normal pancreas cDNA libraries, as described by Hara et al. (Blood, 84:189-199, 1994) with some modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as follows. Normal pancreas cDNA library (70 µg) was digested with EcoRI, NotI, and SfuI, followed by a filling-in reaction with DNA After phenol-chloroform extraction and ethanol polymerase Klenow fragment. precipitation, the DNA was dissolved in 100 µl of H<sub>2</sub>O, heat-denatured and mixed with 100 μl (100 μg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23  $\mu$ l  $H_2O$  to form the driver DNA.

To form the tracer DNA, 10 µg prostate tumor cDNA library was digested with BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 µl H<sub>2</sub>O. Tracer DNA was mixed with 15 µl driver DNA and 20 µl of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% 25 sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12  $\mu$ l H<sub>2</sub>O, mixed with 8  $\mu$ l driver DNA and 20 µl of 2 x hybridization buffer, and subjected to a hybridization at 68

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<sup>0</sup>C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK<sup>+</sup> (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction 1").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively, with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12 (also referred to as P504S). This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108. cDNA splice variants of P504S are provided in SEQ ID NO: 600-605.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes

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in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1 µg each of human glandular kallikrein, PSA and mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6. N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species. (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively). Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to R. norvegicus mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA library with spike, four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEO ID NOS: 32 and 38, respectively) were found to show some homology to nonhuman sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show some homology to known human sequences. No significant homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, and the consulting and the companion of the control of the construction of the constru respectively).

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Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding predicted amino acid sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S. A cDNA splice variant of P501S is provided in SEQ ID NO: 606.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A+ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein, mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in SEQ ID NOS: 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the

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isolated clones led to the determination of extended cDNA sequences for 1G-4736. 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807, 1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS: 179-188 and 191-193, respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were over-expressed in most prostate tumors and prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the identification of six additional clones referred to as 1G-4761, 1G-4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 199, respectively, and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA+RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297, 1D-4309, 1D.1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 30 103 and 104, respectively). Further analysis of the isolated clones led to the

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determination of extended cDNA sequences for 1D-4309, 1D.1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in 5 prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni, Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. 10 microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be overexpressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, 15 bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously 20 identified ESTs.

Additional, studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339. Two variant full-length cDNA sequences for P510S are provided in SEQ ID NO: 535 and 536, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 537 and 538, respectively. Additional splice variants of P510S are provided in SEQ ID NO: 598 and 599.

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## **EXAMPLE 2**

## DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE-SPECIFIC POLYPEPTIDES

Using gene specific primers, mRNA expression levels for the representative prostate-specific polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 1-2  $\mu g$  of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42  $^{0}$ C for one hour. The cDNA was then amplified by PCR with genespecific primers. To ensure the semi-quantitative nature of the RT-PCR,  $\beta$ -actin was used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed using  $\beta$ -actin specific primers. A dilution was then chosen that enabled the linear range amplification of the  $\beta$ -actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the  $\beta$ -actin levels were determined for each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in four different types of tumor tissue (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found to be expressed at high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin,

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small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at low to undetectable levels in all the other tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also expressed in breast and colon tumors, but was not detectable in normal tissues.

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RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH prostates, and normal colon, kidney, liver, lung, pancrease, skeletal muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and kidney, but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following normal tissues: prostate, liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be

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over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-expressed in prostate tumor and normal prostate, expressed at lower levels in normal spinal cord, and to be undetectable in all other tissues tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatzis et al. (Proc. Natl. Acad. Sci. USA 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney. The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was found to show some homology to the previously isolated Human mRNA for JM27 protein. Subsequent comparison of the sequence of SEQ ID NO: 384 with sequences in the public databases, led to the identification of a full-length cDNA sequence of P1000C (SEQ ID NO: 786), which encodes a 492 amino acid sequence. Analysis of the amino acid sequence using the PSORT II program led to the

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identification of a putative transmembrane domain from amino acids 84-100. The cDNA sequence of the open reading frame of P1000C, including the stop codon, is provided in SEQ ID NO: 787, with the open reading frame without the stop codon being provided in SEQ ID NO: 788. The full-length amino acid sequence of P1000C is provided in SEQ ID NO: 789. SEQ ID NO: 790 and 791 represent amino acids 1-100 and 100-492 of P1000C, respectively.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver, brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

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## **EXAMPLE 3**

# ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA subtraction library, containing cDNA from normal prostate subtracted with ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' E. coli (Stratagene). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

Fifty-nine positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

Further studies employing the sequence of SEQ ID NO: 67 as a probe in standard full-length cloning methods, resulted in the isolation of three cDNA sequences which appear to be splice variants of P80 (also known as P704P). These sequences are provided in SEQ ID NO: 620-622.

Further studies using the PCR-based methodology described above resulted in the isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145,

147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161-170) were found to have some degree of homology to known genes. Larger cDNA clones containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA sequence for an extended spliced form of P703 is provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary (n=2), skeletal muscle, skin, stomach, small intestine and brain), and activated and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed comparable expression. P20, a portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of 2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal prostate and prostate tumor, compared to six of twelve other normal tissues tested.

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Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. However, substantial expression of P29 was observed in normal colon and normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-h11, 9-f12 and 9-f3. The determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

mRNA expression levels for these clones were determined using the micro-array technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable. Increased expression of 8-F11 was seen in prostate tumor and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.

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An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both microarray technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those in the public databases revealed 99% identity to the known gene HOXB13.

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Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

10 PCR and hybridization-based methodologies were employed to obtain longer cDNA sequences for clone P20 (also referred to as P703P), vielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEO ID NO: 326. 328 and 330, with the predicted corresponding amino acid sequences being provided in SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. 15 P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX 23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of 20 the putative signal sequence. The full-length cDNA sequence for P703P is provided in SEQ ID NO: 524, with the corresponding amino acid sequence being provided in SEQ ID NO: 525.

Using computer algorithms, the following regions of P703P were predicted to represent potential HLA A2-binding CTL epitopes: amino acids 164-172 of SEQ ID NO: 525 (SEQ ID NO: 723); amino acids 160-168 of SEQ ID NO: 525 (SEQ ID NO: 525); amino acids 118-126 of SEQ ID NO: 525 (SEQ ID NO: 726); amino acids 118-126 of SEQ ID NO: 525 (SEQ ID NO: 726); amino acids 112-120 of SEQ ID NO: 525 (SEQ ID NO: 727); amino acids 155-164 of SEQ ID NO: 525 (SEQ ID NO: 728); amino acids 117-126 of SEQ ID NO: 525 (SEQ ID NO: 729); amino acids 164-173 of SEQ ID NO: 525 (SEQ ID NO: 730); amino acids 154-163 of SEQ ID NO:

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525 (SEQ ID NO: 731); amino acids 163-172 of SEQ ID NO: 525 (SEQ ID NO: 732); amino acids 58-66 of SEQ ID NO: 525 (SEQ ID NO: 733); and amino acids 59-67 of SEQ ID NO: 525 (SEQ ID NO: 734).

P703P was found to show some homology to previously identified proteases, such as thrombin. The thrombin receptor has been shown to be preferentially expressed in highly metastatic breast carcinoma cells and breast carcinoma biopsy samples. Introduction of thrombin receptor antisense cDNA has been shown to inhibit the invasion of metastatic breast carcinoma cells in culture. Antibodies against thrombin receptor inhibit thrombin receptor activation and thrombin-induced platelet activation. Furthermore, peptides that resemble the receptor's tethered ligand domain inhibit platelet aggregation by thrombin. P703P may play a role in prostate cancer through a protease-activated receptor on the cancer cell or on stromal cells. potential trypsin-like protease activity of P703P may either activate a protease-activated receptor on the cancer cell membrane to promote tumorgenesis or activate a proteaseactivated receptor on the adjacent cells (such as stromal cells) to secrete growth factors and/or proteases (such as matrix metalloproteinases) that could promote tumor angiogenesis, invasion and metastasis. P703P may thus promote tumor progression and/or metastasis through the activation of protease-activated receptor. Polypeptides and antibodies that block the P703P-receptor interaction may therefore be usefully employed in the treatment of prostate cancer.

To determine whether P703P expression increases with increased severity of Gleason grade, an indicator of tumor stage, quantitative PCR analysis was performed on prostate tumor samples with a range of Gleason scores from 5 to > 8. The mean level of P703P expression increased with increasing Gleason score, indicating that P703P expression may correlate with increased disease severity.

Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are

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provided in SEQ ID NO: 307-311, 313 and 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold over-expression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal prostate tissues (n=4), but background to low expression levels in all normal tissues. Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

Further studies led to the isolation of an extended cDNA sequence for P712P (SEQ ID NO: 552). The amino acid sequences encoded by 16 predicted open reading frames present within the sequence of SEQ ID NO: 552 are provided in SEQ ID NO: 553-568.

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the cDNAs which were picked up by these filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no significant homologies to P714P

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were found. Further studies employing the sequence of SEQ ID NO: 334 as a probe in standard full-length cloning methods, resulted in an extended cDNA sequence for P714P. This sequence is provided in SEQ ID NO: 619. This sequence was found to show some homology to the gene that encodes human ribosomal L23A protein.

Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

Further studies on P775P resulted in the isolation of four additional sequences (SEQ ID NO: 473-476) which are all splice variants of the P775P gene. The sequence of SEQ ID NO: 474 was found to contain two open reading frames (ORFs). The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 477 and 478. The cDNA sequence of SEQ ID NO: 475 was found to contain an ORF which encodes the amino acid sequence of SEQ ID NO: 479. The cDNA sequence of SEQ ID NO: 473 was found to contain four ORFs. The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 480-483. Additional splice variants of P775P are provided in SEQ ID NO: 593-597.

Subsequent studies led to the identification of a genomic region on chromosome 22q11.2, known as the Cat Eye Syndrome region, that contains the five prostate genes P704P, P712P, P774P, P775P and B305D. The relative location of each of these five genes within the genomic region is shown in Fig. 10. This region may therefore be associated with malignant tumors, and other potential tumor genes may be contained within this region. These studies also led to the identification of a potential open reading frame (ORF) for P775P (provided in SEQ ID NO: 533), which encodes the amino acid sequence of SEQ ID NO: 534.

Comparison of the clone of SEQ ID NO: 325 (referred to as P558S) with sequences in the GenBank and GeneSeq DNA databases showed that P558S is identical to the prostate-specific transglutaminase gene, which is known to have two forms. The full-length sequences for the two forms are provided in SEQ ID NO: 630 and 631, with the corresponding amino acid sequences being provided in SEQ ID NO: 632 and 633, respectively. The cDNA sequence of SEQ ID NO: 631 has a 15 pair base insert, resulting in a 5 amino acid insert in the corresponding amino acid sequence (SEQ ID NO: 633). This insert is not present in the sequence of SEQ ID NO: 630.

Further studies on P768P (SEQ ID NO: 315) led to the identification of the putative full-length open reading frame (ORF). The cDNA sequence of the ORF with stop codon is provided in SEQ ID NO: 764. The cDNA sequence of the ORF without stop codon is provided in SEQ ID NO: 765, with the corresponding amino acid sequence being provided in SEQ ID NO: 766. This sequence was found to show 86% identity to a rat calcium transporter protein, indicating that P768P may represent a human calcium transporter protein. The locations of transmembrane domains within P768P were predicted using the PSORT II computer algorithm. Six transmembrane domains were predicted at amino acid positions 118-134, 172-188, 211-227, 230-246, 282-298 and 348-364. The amino acid sequences of SEQ ID NO: 767-772 represent amino acids 1-134, 135-188, 189-227, 228-246, 247-298 and 299-511 of P768P, respectively.

## **EXAMPLE 4**

## SYNTHESIS OF POLYPEPTIDES

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Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using FMOC chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of

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0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1 % TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

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## EXAMPLE 5

## FURTHER ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that recognize six-nucleotide 15 restriction sites (Mlul, Mscl, Pvull, Sall and Stul). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

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This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JPTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat norvegicus cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to G. gallus dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most recent release of GenBank revealed no significant homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most prostate tumors and BPH tissues by a factor of three or greater, with elevated expression

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seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low expression in all other normal tissues tested.

Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be overexpressed in prostate tumor. The clones of SEQ ID NO: 341, 342, 345, 347, 348, 349, 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 11 (SEQ ID NO: 340-349 and 362) were found to show some homology to previously identified sequences. No significant homologies were found to the clones of SEQ ID NO: 350, 351, 353-361, and 363-365.

Comparison of the sequence of SEQ ID NO: 362 with sequences in the GenBank and GeneSeq DNA databases showed that this clone (referred to as P788P) is identical to GeneSeq Accession No. X27262, which encodes a protein found in the GeneSeq protein Accession No. Y00931. The full length cDNA sequence of P788P is provided in SEQ ID NO: 634, with the corresponding predicted amino acid being provided in SEQ ID NO: 635. Subsequently, a full-length cDNA sequence for P788P that contains polymorphisms not found in the sequence of SEQ ID NO: 634, was cloned multiple times by PCR amplification from cDNA prepared from several RNA templates from three individuals. This determined cDNA sequence of this polymorphic variant of P788P is provided in SEQ ID NO: 636, with the corresponding amino acid sequence being provided in SEQ ID NO: 637. The sequence of SEQ ID NO: 637 differs from that of SEQ ID NO: 635 by six amino acid residues. The P788P protein has 7 potential transmembrane domains at the C-terminal portion and is predicted to be a plasma membrane protein with an extracellular N-terminal region.

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Further studies on the clone of SEQ ID NO: 352 (referred to as P790P) led to the isolation of the full-length cDNA sequence of SEQ ID NO: 526. The corresponding predicted amino acid is provided in SEQ ID NO: 527. Data from two quantitative PCR experiments indicated that P790P is over-expressed in 11/15 tested prostate tumor samples and is expressed at low levels in spinal cord, with no expression being seen in all other normal samples tested. Data from further PCR experiments and microarray experiments showed over-expression in normal prostate and prostate tumor with little or no expression in other tissues tested. P790P was subsequently found to show significant homology to a previously identified G-protein coupled prostate tissue receptor.

Additional studies on the clone of SEQ ID NO: 354 (referred to as P776P) led to the isolation of an extended cDNA sequence, provided in SEO ID NO: 569. The determined cDNA sequences of three additional splice variants of P776P are provided in SEQ ID NO: 570-572. The amino acid sequences encoded by two predicted open reading frames (ORFs) contained within SEQ ID NO: 570, one predicted ORF contained within SEQ ID NO: 571, and 11 predicted ORFs contained within SEQ ID NO: 569, are provided in SEQ ID NO: 573-586, respectively. Further studies led to the isolation of the full-length sequence for the clone of SEQ ID NO: 570 (provided in SEQ ID NO: 737). Full-length cloning efforts on the clone of SEQ ID NO: 571 led to the isolation of two sequences (provided in SEQ ID NO: 738 and 739), representing a single clone, that are identical with the exception of a polymorphic insertion/deletion at position 1293. Specifically, the clone of SEQ ID NO: 739 (referred to as clone F1) has a C at position 1293. The clone of SEQ ID NO: 738 (referred to as clone F2) has a single base pair deletion at position 1293. The predicted amino acid sequences encoded by 5 open reading frames located within SEQ ID NO: 737 are provided in SEQ ID NO: 740-744, with the predicted amino acid sequences encoded by the clone of SEQ ID NO: 738 and 739 being provided in SEQ ID NO: 745-750.

Comparison of the cDNA sequences for the clones P767P (SEQ ID NO: 314) and P777P (SEQ ID NO: 350) with sequences in the GenBank human EST database showed that the two clones matched many EST sequences in common,

suggesting that P767P and P777P may represent the same gene. A DNA consensus sequence derived from a DNA sequence alignment of P767P, P777P and multiple EST clones is provided in SEQ ID NO: 587. The amino acid sequences encoded by three putative ORFs located within SEQ ID NO: 587 are provided in SEQ ID NO: 588-590.

The clone of SEQ ID NO: 342 (referred to as P789P) was found to show homology to a previously identified gene. The full length cDNA sequence for P789P and the corresponding amino acid sequence are provided in SEQ ID NO: 735 and 736, respectively.

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#### **EXAMPLE 6**

### PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

Mice expressing the transgene for human HLA A2Kb (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID NO: 8), as described by Theobald et al., Proc. Natl. Acad. Sci. USA 92:11993-11997, 1995 with the following modifications. Mice were immunized with 100µg of P2S#12 and 120µg of an I-Ab binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at 6 x 10<sup>6</sup> cells/ml in complete media (RPMI-1640; Gibco BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL), 2 x 10<sup>-5</sup> M 2mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml  $\beta$ 2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later, cells (5 x 105/ml) were restimulated with 2.5 x 10<sup>6</sup>/ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells

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(Sherman et al, Science 258:815-818, 1992) and 3 x 10<sup>6</sup>/ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

P2S#12 line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells (1 x 10<sup>4</sup> cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5 x 10<sup>5</sup> cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2Kb expressing) transduced with P502S than against control fibroblasts. An example is presented in Figure 1.

This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2Kb molecule.

6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, et al, J. Immunol., 152:163, 1994). P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2 binding using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200 µg/ml were added to cultures of D150M58 CTL in order to bind HLA-A2 on the CTL. After thirty minutes,

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CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

Mice expressing the transgene for human HLA A2Kb were immunized as described by Theobald et al. (Proc. Natl. Acad. Sci. USA 92:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5µg of P1S #10 and 120µg of an I-Ab binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared using a nylon mesh. Cells were then resuspended at 6 x 10<sup>6</sup> cells/ml in complete media (as described above) and cultured in the presence of irradiated (3000 rads) P1S#10-pulsed (2µg/ml P1S#10 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later cells (5 x 10<sup>5</sup>/ml) were restimulated with 2.5 x 10<sup>6</sup>/ml peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and 3 x 10<sup>6</sup>/ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20 U/ml IL-2. Cells were restimulated on a weekly basis in preparation for cloning. After three rounds of in vitro stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as 20 shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells (1 x 10<sup>4</sup> cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5 x 10<sup>5</sup> cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were isolated and maintained in culture. As shown in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2Kb targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

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#### **EXAMPLE 7**

#### PRIMING OF CTL IN VIVO USING NAKED DNA IMMUNIZATION

#### WITH A PROSTATE ANTIGEN

The prostate-specific antigen L1-12, as described above, is also referred to as P501S. HLA A2Kb Tg mice (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with 100 µg P501S in the vector VR1012 either intramuscularly or intradermally. The mice were immunized three times, with a two week interval between immunizations. Two weeks after the last immunization, immune spleen cells were cultured with Jurkat A2Kb-P501S transduced stimulator cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL activity was assessed against P501S transduced targets. Two out of 8 mice developed strong anti-P501S CTL responses. These results demonstrate that P501S contains at least one naturally processed HLA-A2-restricted CTL epitope.

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#### **EXAMPLE 8**

#### ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE-SPECIFIC POLYPEPTIDES

This Example illustrates the ability of T cells specific for a prostate tumor polypeptide to recognize human tumor.

Human CD8<sup>+</sup> T cells were primed *in vitro* to the P2S-12 peptide (SEQ ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells according to the protocol of Van Tsai et al. (*Critical Reviews in Immunology 18*:65-75, 1998). The resulting CD8<sup>+</sup> T cell microcultures were tested for their ability to recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which were transduced to express the P502S gene in a γ-interferon ELISPOT assay (*see* Lalvani et al., *J. Exp. Med. 186*:859-865, 1997). Briefly, titrating numbers of T cells were assayed in duplicate on 10<sup>4</sup> fibroblasts in the presence of 3 μg/ml human β<sub>2</sub>-microglobulin and 1 μg/ml P2S-12 peptide or control E75 peptide. In addition, T cells were simultaneously assayed on autologous fibroblasts transduced with the P502S gene or as a control, fibroblasts transduced with HER-2/neu. Prior to the assay, the

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fibroblasts were treated with 10 ng/ml γ-interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a γ-interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of  $\gamma$ -interferon spots with increasing numbers of T cells on fibroblasts pulsed with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of yinterferon spots with increasing numbers of T cells on fibroblasts transduced to express the P502S gene but not the HER-2/neu gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene. 

#### **EXAMPLE 9**

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# ELICITATION OF PROSTATE ANTIGEN-SPECIFIC CTL RESPONSES IN HUMAN BLOOD

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This Example illustrates the ability of a prostate-specific antigen to elicit a CTL response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing 10% human serum, 50 ng/ml GMCSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8+ cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles using autologous fibroblasts

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retrovirally transduced to express P501S and CD80, CD8+ lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-The P501S-specific activity of cell line 3A-1 could be transduced fibroblasts. maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL transduced to express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxicity assays (<sup>51</sup>Cr release) and interferon-gamma production (Interferongamma Elispot; see above and Lalvani et al., J. Exp. Med. 186:859-865, 1997). The results of these assays are presented in Figures 6A and 6B.

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#### EXAMPLE 10

# IDENTIFICATION OF A NATURALLY PROCESSED CTL EPITOPE CONTAINED WITHIN THE PROSTATE-SPECIFIC ANTIGEN P703P

The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific human CD8+ T cells can be primed following repeated in vitro stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed and P703P-transduced target cells in both ELISPOT (as described above) and chromium release assays. Additionally, 20 immunization of HLA-A2Kb transgenic mice with p5 leads to the generation of CTL lines which recognize a variety of HLA-A2Kb or HLA-A2 transduced target cells expressing P703P.

Initial studies demonstrating that p5 is a naturally processed epitope were done using HLA-A2Kb transgenic mice. HLA-A2Kb transgenic mice were immunized 25 subcutaneously in the footpad with 100 µg of p5 peptide together with 140 µg of hepatitis B virus core peptide (a Th peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated in vitro with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay 30 five days after primary in vitro stimulation. Retrovirally transduced cells expressing the

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control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were identified.

Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by culturing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, the DC were pulsed with 1 ug/ml p5 peptide and cultured with CD8+ T cell enriched PBMC. CTL lines were restimulated on a weekly basis with p5-pulsed monocytes. Five to six weeks after initiation of the CTL cultures, CTL recognition of p5-pulsed target cells was demonstrated. CTL were additionally shown to recognize human cells transduced to express P703P, demonstrating that p5 is a naturally processed epitope.

Studies identifying a further peptide epitope (referred to as peptide 4) derived from the prostate tumor-specific antigen P703P that is capable of being recognized by CD4 T cells on the surface of cells in the context of HLA class II molecules were carried out as follows. The amino acid sequence for peptide 4 is provided in SEQ ID NO: 638, with the corresponding cDNA sequence being provided in SEQ ID NO: 639.

Twenty 15-mer peptides overlapping by 10 amino acids and derived from the carboxy-terminal fragment of P703P were generated using standard 20 procedures. Dendritic cells (DC) were derived from PBMC of a normal female donor using GM-CSF and IL-4 by standard protocols. CD4 T cells were generated from the same donor as the DC using MACS beads and negative selection. DC were pulsed overnight with pools of the 15-mer peptides, with each peptide at a final concentration 25 of 0.25 microgram/ml. Pulsed DC were washed and plated at 1 x 10<sup>4</sup> cells/well of 96well V-bottom plates and purified CD4 T cells were added at 1 x 10<sup>5</sup>/well. Cultures were supplemented with 60 ng/ml IL-6 and 10 ng/ml IL-12 and incubated at 37 °C. Cultures were restimulated as above on a weekly basis using DC generated and pulsed as above as antigen presenting cells, supplemented with 5 ng/ml IL-7 and 10 u/ml IL-2. Following 4 in vitro stimulation cycles, 96 lines (each line corresponding to one well) 30 were tested for specific proliferation and cytokine production in response to the

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stimulating pools with an irrelevant pool of peptides derived from mammaglobin being used as a control.

One line (referred to as 1-F9) was identified from pool #1 that demonstrated specific proliferation (measured by 3H proliferation assays) and cytokine production (measured by interferon-gamma ELISA assays) in response to pool #1 of P703P peptides. This line was further tested for specific recognition of the peptide pool, specific recognition of individual peptides in the pool, and in HLA mismatch analyses to identify the relevant restricting allele. Line 1-F9 was found to specifically proliferate and produce interferon-gamma in response to peptide pool #1, and also to peptide 4 (SEQ ID NO: 638). Peptide 4 corresponds to amino acids 126-140 of SEQ ID NO: 327. Peptide titration experiments were conducted to assess the sensitivity of line 1-F9 for the specific peptide. The line was found to specifically respond to peptide 4 at concentrations as low as 0.25 ng/ml, indicating that the T cells are very sensitive and therefore likely to have high affinity for the epitope.

To determine the HLA restriction of the P703P response, a panel of antigen presenting cells (APC) was generated that was partially matched with the donor used to generate the T cells. The APC were pulsed with the peptide and used in proliferation and cytokine assays together with line 1-F9. APC matched with the donor at HLA-DRB0701 and HLA-DQB02 alleles were able to present the peptide to the T cells, indicating that the P703P-specific response is restricted to one of these alleles.

Antibody blocking assays were utilized to determine if the restricting allele was HLA-DR0701 or HLA-DQ02. The anti-HLA-DR blocking antibody L243 or an irrelevant isotype matched IgG2a were added to T cells and APC cultures pulsed with the peptide RMPTVLQCVNVSVVS (SEQ ID NO: 638) at 250 ng/ml. Standard interferon-gamma and proliferation assays were performed. Whereas the control antibody had no effect on the ability of the T cells to recognize peptide-pulsed APC, in both assays the anti-HLA-DR antibody completely blocked the ability of the T cells to specifically recognize peptide-pulsed APC.

To determine if the peptide epitope RMPTVLQCVNVSVVS (SEQ ID NO: 638) was naturally processed, the ability of line 1-F9 to recognize APC pulsed with recombinant P703P protein was examined. For these experiments a number of

recombinant P703P sources were utilized; E. coli-derived P703P, Pichia-derived P703P and baculovirus-derived P703P. Irrelevant protein controls used were E. coli-derived L3E a lung-specific antigen) and baculovirus-derived mammaglobin. In interferongamma ELISA assays, line 1-F9 was able to efficiently recognize both E. coli forms of P703P as well as Pichia-derived recombinant P703P, while baculovirus-derived P703P was recognized less efficiently. Subsequent Western blot analysis revealed that the E coli and Pichia P703P protein preparations were intact while the baculovirus P703P preparation was approximately 75% degraded. Thus, peptide RMPTVLQCVNVSVVS (SEQ ID NO: 638) from P703P is a naturally processed peptide epitope derived from 10 P703P and presented to T cells in the context of HLA-DRB-0701

In further studies, twenty-four 15-mer peptides overlapping by 10 amino acids and derived from the N-terminal fragment of P703P (corresponding to amino acids 27-154 of SEQ ID NO: 525) were generated by standard procedures and their ability to be recognized by CD4 cells was determined essentially as described above. 15 DC were pulsed overnight with pools of the peptides with each peptide at a final concentration of 10 microgram/ml. A large number of individual CD4 T cell lines (65/480) demonstrated significant proliferation and cytokine release (IFN-gamma) in response to the P703P peptide pools but not to a control peptide pool. The CD4 T cell lines which demonstrated specific activity were restimulated on the appropriate pool of P703P peptides and reassayed on the individual peptides of each pool as well as a peptide dose titration of the pool of peptides in a IFN-gamma release assay and in a proliferation assay.

Sixteen immunogenic peptides were recognized by the T cells from the entire set of peptide antigens tested. The amino acid sequences of these peptides are provided in SEQ ID NO: 656-671, with the corresponding cDNA sequences being provided in SEQ ID NO: 640-655, respectively. In some cases the peptide reactivity of the T cell line could be mapped to a single peptide, however some could be mapped to more than one peptide in each pool. Those CD4 T cell lines that displayed a representative pattern of recognition from each peptide pool with a reasonable affinity for peptide were chosen for further analysis (I-1A, -6A; II-4C, -5E; III-6E, IV-4B, -3F, -9B, -10F, V-5B, -4D, and -10F). These CD4 T cells lines were restimulated on the

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appropriate individual peptide and reassayed on autologous DC pulsed with a truncated form of recombinant P703P protein made in E. coli (a.a. 96 - 254 of SEQ ID NO: 525), full-length P703P made in the baculovirus expression system, and a fusion between influenza virus NS1 and P703P made in E. coli. Of the T cell lines tested, line I-1A recognized specifically the truncated form of P703P (E. coli) but no other recombinant form of P703P. This line also recognized the peptide used to elicit the T cells. Line 2-4C recognized the truncated form of P703P (E. coli) and the full length form of P703P made in baculovirus, as well as peptide. The remaining T cell lines tested were either peptide-specific only (II-5E, II-6F, IV-4B, IV-3F, IV-9B, IV-10F, V-5B and V-4D) or were non-responsive to any antigen tested (V-10F). These results demonstrate that the peptide sequence RPLLANDLMLIKLDE (SEQ ID NO: 671; corresponding to a.a. 110-124 of SEQ ID NO: 525) recognized by the T cell line I-1A, and the peptide sequences SVSESDTIRSISIAS (SEQ ID NO: 668; corresponding to a.a. 125-139 of SEQ ID NO: 525) and ISIASQCPTAGNSCL (SEQ ID NO: 667; corresponding to a.a. 135-149 of SEQ ID NO: 525) recognized by the T cell line II-4C may be naturally processed epitopes of the P703P protein.

#### **EXAMPLE 11**

# EXPRESSION OF A BREAST TUMOR-DERIVED ANTIGEN IN PROSTATE

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Isolation of the antigen B305D from breast tumor by differential display is described in US Patent Application No. 08/700,014, filed August 20, 1996. Several different splice forms of this antigen were isolated. The determined cDNA sequences for these splice forms are provided in SEQ ID NO: 366-375, with the predicted amino acid sequences corresponding to the sequences of SEQ ID NO: 292, 298 and 301-303 being provided in SEQ ID NO: 299-306, respectively. In further studies, a splice variant of the cDNA sequence of SEQ ID NO: 366 was isolated which was found to contain an additional guanine residue at position 884 (SEQ ID NO: 530), leading to a 30 frameshift in the open reading frame. The determined DNA sequence of this ORF is

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provided in SEO ID NO: 531. This frameshift generates a protein sequence (provided in SEQ ID NO: 532) of 293 amino acids that contains the C-terminal domain common to the other isoforms of B305D but that differs in the N-terminal region.

The expression levels of B305D in a variety of tumor and normal tissues were examined by real time PCR and by Northern analysis. The results indicated that B305D is highly expressed in breast tumor, prostate tumor, normal prostate and normal testes, with expression being low or undetectable in all other tissues examined (colon tumor, lung tumor, ovary tumor, and normal bone marrow, colon, kidney, liver, lung, ovary, skin, small intestine, stomach). Using real-time PCR on a panel of prostate tumors, expression of B305D in prostate tumors was shown to increase with increasing Gleason grade, demonstrating that expression of B305D increases as prostate cancer م بألم تسميل ترافق إلى المؤلول progresses. BOOK AND A CONTRACT POINT

# EXAMPLE 12

GENERATION OF HUMAN CTL IN VITRO USING WHOLE GENE PRIMING AND STIMULATION TECHNIQUES WITH THE PROSTATE-SPECIFIC ANTIGEN P501S

Using in vitro whole-gene priming with P501S-vaccinia infected DC (see, for example, Yee et al, The Journal of Immunology, 157(9):4079-86, 1996), human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon-y ELISPOT Using a panel of HLA-mismatched B-LCL lines analysis as described above. transduced with P501S, these CTL lines were shown to be likely restricted to HLAB class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3 µg/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8+ 30 T cells were isolated using a magnetic bead system, and priming cultures were initiated

using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S and CD80. Following four stimulation cycles, CD8+ T cell lines were identified that specifically produced interferon-γ when stimulated with P501S and CD80-transduced autologous fibroblasts. A panel of HLA-mismatched B-LCL lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon-γ in an ELISPOT assay, the P501S specific response was shown to be likely restricted by HLA B alleles. These results demonstrate that a CD8+ CTL response to P501S can be elicited.

10 To identify the epitope(s) recognized, cDNA encoding P501S was fragmented by various restriction digests, and sub-cloned into the retroviral expression vector pBIB-KS. Retroviral supernatants were generated by transfection of the helper packaging line Phoenix-Ampho. Supernatants were then used to transduce Jurkat/A2Kb cells for CTL screening. CTL were screened in IFN-gamma ELISPOT assays against these A2Kb targets transduced with the "library" of P501S fragments. 15 Initial positive fragments P501S/H3 and P501S/F2 were sequenced and found to encode amino acids 106-553 and amino acids 136-547, respectively, of SEQ ID NO: 113. A truncation of H3 was made to encode amino acid residues 106-351 of SEQ ID NO: 113, which was unable to stimulate the CTL, thus localizing the epitope to amino acid residues 351-547. Additional fragments encoding amino acids 1-472 (Fragment A) and amino acids 1-351 (Fragment B) were also constructed. Fragment A but not Fragment B stimulated the CTL thus localizing the epitope to amino acid residues 351-472. Overlapping 20-mer and 18-mer peptides representing this region were tested by pulsing Jurkat/A2Kb cells versus CTL in an IFN-gamma assay. Only peptides P501S-369(20) 25 and P501S-369(18) stimulated the CTL. Nine-mer and 10-mer peptides representing this region were synthesized and similarly tested. Peptide P501S-370 (SEQ ID NO: 539) was the minimal 9-mer giving a strong response. Peptide P501S-376 (SEQ ID NO: 540) also gave a weak response, suggesting that it might represent a cross-reactive epitope.

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In subsequent studies, the ability of primary human B cells transduced with P501S to prime MHC class I-restricted, P501S-specific, autologous CD8 T cells was examined. Primary B cells were derived from PBMC of a homozygous HLA-A2 donor by culture in CD40 ligand and IL-4, transduced at high frequency with recombinant P501S in the vector pBIB, and selected with blastocidin-S. For in vitro priming, purified CD8+ T cells were cultured with autologous CD40 ligand + IL-4 derived, P501S-transduced B cells in a 96-well microculture format. These CTL microcultures were re-stimulated with P501S-transduced B cells and then assayed for specificity. Following this initial screen, microcultures with significant signal above background were cloned on autologous EBV-transformed B cells (BLCL), also transduced with P501S. Using IFN-gamma ELISPOT for detection, several of these CD8 T cell clones were found to be specific for P501S, as demonstrated by reactivity to BLCL/P501S but not BLCL transduced with control antigen. It was further demonstrated that the anti-P501S CD8 T cell specificity is HLA-A2-restricted. First, antibody blocking experiments with anti-HLA-A,B,C monoclonal antibody (W6.32), anti-HLA-B,C monoclonal antibody (B1.23.2) and a control monoclonal antibody showed that only the anti-HLA-A,B,C antibody blocked recognition of P501Sexpressing autologous BLCL. Secondly, the anti-P501S CTL also recognized an HLA-A2 matched, heterologous BLCL transduced with P501S, but not the corresponding EGFP transduced control BLCL.

A naturally processed, CD8, class I-restricted peptide epitope of P501S was identified as follows. Dendritic Cells (DC) were isolated by Percol gradient followed by differential adherence, and cultured for 5 days in the presence of RPMI medium containing 1% human serum, 50ng/ml GM-CSF and 30ng/ml IL-4. Following culture, DC were infected for 24 hours with P501S-expressing adenovirus at an MOI of 10 and matured for an additional 24 hours by the addition of 2ug/ml CD40 ligand. CD8 cells were enriched for by the subtraction of CD4+, CD14+ and CD16+ populations from PBMC with magnetic beads. Priming cultures containing 10,000 P501Sexpressing DC and 100,000 CD8+ T cells per well were set up in 96-well V-bottom plates with RPMI containing 10% human serum, 5ng/ml IL-12 and 10ng/ml IL-6. Cultures were stimulated every 7 days using autologous fibroblasts retrovirally

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transduced to express P501S and CD80, and were treated with IFN-gamma for 48-72 hours to upregulate MHC Class I expression. 10u/ml IL-2 was added at the time of stimulation and on days 2 and 5 following stimulation. Following 4 stimulation cycles, one P501S-specific CD8+ T cell line (referred to as 2A2) was identified that produced IFN-gamma in response to IFN-gamma-treated P501S/CD80 expressing autologous fibroblasts, but not in response to IFN-gamma-treated P703P/CD80 expressing autologous fibroblasts in a γ-IFN Elispot assay. Line 2A2 was cloned in 96-well plates with 0.5 cell/well or 2 cells/well in the presence of 75,000 PBMC/well, 10,000 B-LCL/well, 30ng/ml OKT3 and 50u/ml IL-2. Twelve clones were isolated that showed strong P501S specificity in response to transduced fibroblasts.

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Fluorescence activated cell sorting (FACS) analysis was performed on P501S-specific clones using CD3-, CD4- and CD8-specific antibodies conjugated to PercP, FITC and PE respectively. Consistent with the use of CD8 enriched T cells in the priming cultures, P5401S-specific clones were determined to be CD3+, CD8+ and CD4-.

To identify the relevant P501S epitope recognized by P501S specific CTL, pools of 18-20 mer or 30-mer peptides that spanned the majority of the amino acid sequence of P501S were loaded onto autologous B-LCL and tested in y-IFN Elispot assays for the ability to stimulate two P501S-specific CTL clones, referred to as 4E5 and 4E7. One pool, composed of five 18-20 mer peptides that spanned amino acids 411-486 of P501S (SEQ ID NO: 113), was found to be recognized by both P501S-specific clones. To identify the specific 18-20 mer peptide recognized by the clones, each of the 18-20 mer peptides that comprised the positive pool were tested individually in γ-IFN Elispot assays for the ability to stimulate the two P501S-specific CTL clones, 4E5 and 4E7. Both 4E5 and 4E7 specifically recognized one 20-mer peptide (SEQ ID NO: 710: cDNA sequence provided in SEQ ID NO: 711) that spanned amino acids 453-472 of P501S. Since the minimal epitope recognized by CD8+ T cells is almost always either a 9 or 10-mer peptide sequence, 10-mer peptides that spanned the entire sequence of SEO ID NO: 710 were synthesized that differed by 1 amino acid. Each of these 10-mer 30 peptides was tested for the ability to stimulate two P501S-specific clones, (referred to as 1D5 and 1E12). One 10-mer peptide (SEQ ID NO: 712; cDNA sequence provided in

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SEQ ID NO: 713) was identified that specifically stimulated the P501S-specific clones. This epitope spans amino acids 463-472 of P501S. This sequence defines a minimal 10mer epitope from P501S that can be naturally processed and to which CTL responses can be identified in normal PBMC. Thus, this epitope is a candidate for use as a vaccine moiety, and as a therapeutic and/or diagnostic reagent for prostate cancer.

To identify the class I restriction element for the P501S-derived sequence of SEQ ID NO: 712, HLA blocking and mismatch analyses were performed. In γ-IFN Elispot assays, the specific response of clones 4A7 and 4E5 to P501S-transduced autologous fibroblasts was blocked by pre-incubation with 25ug/ml W6/32 (pan-Class I blocking antibody) and B1.23.2 (HLA-B/C blocking antibody). These results demonstrate that the SEQ ID NO: 712-specific response is restricted to an HLA-B or HLA-C allele.

For the HLA mismatch analysis, (HLAautologous B-LCL (HLA-**B-LCL** Cw7)... heterologous and A1,A2,B8,B51, Cw1, A2,A3,B18,B51,Cw5,Cw14) that share the HLAB51 allele were pulsed for one hour with 20ug/ml of peptide of SEQ ID NO: 712, washed, and tested in γ-IFN Elispot assays for the ability to stimulate clones 4A7 and 4E5. Antibody blocking assays with the B1.23.2 (HLA-B/C blocking antibody) were also performed. SEQ ID NO: 712-specific response was detected using both the autologous (D326) and heterologous (D107) B-20 LCL, and furthermore the responses were blocked by pre-incubation with 25ug/ml of B1.23.2 HLA-B/C blocking antibody. Together these results demonstrate that the P501S-specific response to the peptide of SEQ ID NO: 712 is restricted to the HLA-B51 class I allele. Molecular cloning and sequence analysis of the HLA-B51 allele from D3326 revealed that the HLA-B51 subtype of D326 is HLA-B51011.

Based on the 10-mer P501S-derived epitope of SEQ ID NO: 712, two 9mers with the sequences of SEQ ID NO: 714 and 715 were synthesized and tested in Elispot assays for the ability to stimulate two P501S-specific CTL clones derived from line 2A2. The 10-mer peptide of SEQ ID NO: 712, as well as the 9-mer peptide of SEQ ID NO: 715, but not the 9-mer peptide of SEQ ID NO: 714, were capable of stimulating the P501S-specific CTL to produce IFN-gamma. These results demonstrate that the peptide of SEQ ID NO: 715 is a 9-mer P501S-derived epitope recognized by P501S-

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specific CTL. The DNA sequence encoding the epitope of SEQ ID NO: 715 is provided in SEQ ID NO: 716.

To identify the class I restricting allele for the P501S-derived peptide of SEQ ID NO: 712 and 715 specific response, each of the HLA B and C alleles were cloned from the donor used in the *in vitro* priming experiment. Sequence analysis indicated that the relevant alleles were HLA-B8, HLA-B51, HLA-Cw01 and HLA-Cw07. Each of these alleles were subcloned into an expression vector and cotransfected together with the P501S gene into VA-13 cells. Transfected VA-13 cells were then tested for the ability to specifically stimulate the P501S-specific CTL in ELISPOT assays. VA-13 cells transfected with P501S and HLA-B51 were capable of stimulating the P501S-specific CTL to secrete gamma-IFN. VA-13 cells transfected with HLA-B51 alone or P501S + the other HLA-alleles were not capable of stimulating the P501S-specific CTL. These results demonstrate that the restricting allele for the P501S-specific response is the HLAB51 allele. Sequence analysis revealed that the subtype of the relevant restricting allele is HLA-B51011.

To determine if the P501S-specific CTL could recognize prostate tumor cells that express P501S, the P501S-positive lines LnCAP and CRL2422 (both expressing "moderate" amounts of P501S mRNA and protein), and PC-3 (expressing low amounts of P501S mRNA and protein), plus the P501S-negative cell line DU-145 were retrovirally transduced with the HLA-B51011 allele that was cloned from the donor used to generate the P501S-specific CTL. HLA-B51011- or EGFP-transduced and selected tumor cells were treated with gamma-interferon and androgen (to upregulate stimulatory functions and P501S, respectively) and used in gamma-interferon Elispot assays with the P501S-specific CTL clones 4E5 and 4E7. Untreated cells were used as a control.

Both 4E5 and 4E7 efficiently and specifically recognized LnCAP and CRL2422 cells that were transduced with the HLA-B51011 allele, but not the same cell lines transduced with EGFP. Additionally, both CTL clones specifically recognized PC-3 cells transduced with HLA-B51011, but not the P501S-negative tumor cell line DU-145. Treatment with gamma-interferon or androgen did not enhance the ability of CTL to recognize tumor cells. These results demonstrate that P501S-specific CTL,

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generated by in vitro whole gene priming, specifically and efficiently recognize prostate tumor cell lines that express P501S.

A naturally processed CD4 epitope of P501S was identified as follows.

CD4 cells specific for P501S were prepared as described above. A series of 16 overlapping peptides were synthesized that spanned approximately 50% of the amino terminal portion of the P501S gene (amino acids 1-325 of SEQ ID NO: 113). For priming, peptides were combined into pools of 4 peptides, pulsed at 4 µg/ml onto dendritic cells (DC) for 24 hours, with TNF-alpha. DC were then washed and mixed with negatively selected CD4+ T cells in 96 well U-bottom plates. Cultures were re-10 stimulated weekly on fresh DC loaded with peptide pools. Following a total of 4 stimulation cycles, cells were rested for an additional week and tested for specificity to APC pulsed with peptide pools using  $\gamma$ -IFN ELISA and proliferation assays. For these assays, adherent monocytes loaded with either the relevant peptide pool at 4ug/ml or an irrelevant peptide at ug/ml were used as APC. T cell lines that demonstrated either specific cytokine secretion or proliferation were then tested for recognition of individual peptides that were present in the pool. T cell lines could be identified from pools A and B that recognized individual peptides from these pools.

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From pool A, lines AD9 and AE10 specifically recognized peptide 1 (SEQ ID NO: 719), and line AF5 recognized peptide 39 (SEQ ID NO: 718). From pool B, line BC6 could be identified that recognized peptide 58 (SEQ ID NO: 717). Each of these lines were stimulated on the specific peptide and tested for specific recognition of the peptide in a titration assay as well as cell lysates generated by infection of HEK 293 cells with adenovirus expressing either P501S or an irrelevant antigen. For these assays, APC-adherent monocytes were pulsed with either 10, 1, or 0.1 µg/ml individual P501S peptides, and DC were pulsed overnight with a 1:5 dilution of adenovirally infected cell lysates. Lines AD9, AE10 and AF5 retained significant recognition of the relevant P501S-derived peptides even at 0.1 mg/ml. Furthermore, line AD9 demonstrated significant (8.1 fold stimulation index) specific activity for lysates from adenovirus-P501S infected cells. These results demonstrate that high affinity CD4 T cell lines can be generated toward P501S-derived epitopes, and that at least a subset of these T cells specific for the P501S derived sequence of SEQ ID NO: 719 are specific for an epitope that is naturally processed by human cells. The DNA sequences encoding the amino acid sequences of SEQ ID NO: 717-719 are provided in SEQ ID NO: 720-722, respectively.

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To further characterize the P501S-specific activity of AD9, the line was cloned using anti-CD3. Three clones, referred to as 1A1, 1A9 and 1F5, were identified that were specific for the P501S-1 peptide (SEQ ID NO: 719). To determine the HLA restriction allele for the P501S-specific response, each of these clones was tested in class II antibody blocking and HLA mismatch assays using proliferation and gamma-interferon assays. In antibody blocking assays and measuring gamma-interferon production using ELISA assays, the ability of all three clones to recognize peptide pulsed APC was specifically blocked by co-incubation with either a pan-class II blocking antibody or a HLA-DR blocking antibody, but not with a HLA-DQ or an irrelevant antibody. Proliferation assays performed simultaneously with the same cells confirmed these results. These data indicate that the P501S-specific response of the clones is restricted by an HLA-DR allele. Further studies demonstrated that the restricting allele for the P501S-specific response is HLA-DRB1501.

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#### **EXAMPLE 13**

# IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS By Microarray Analysis

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table I presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-

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15 400) correspond to known sequences, as shown in Table I.

<u>Table I</u>
<u>Summary of Prostate Tumor Antigens</u>

| Known Genes                                          | Previously Identified Genes                   | Novel Genes              |
|------------------------------------------------------|-----------------------------------------------|--------------------------|
| T-cell gamma chain                                   | P504S                                         | 23379 (SEQ ID NO:389)    |
| Kallikrein                                           | P1000C                                        | 23399 (SEQ ID NO:392)    |
| Vector                                               | P501S                                         | 23320 (SEQ ID NO:386)    |
| CGI-82 protein mRNA (23319; SEQ ID NO:385)           | P503S                                         | 23381 (SEQ ID<br>NO:390) |
| PSA                                                  | P510S                                         |                          |
| Ald. 6 Dehyd.                                        | P784P                                         |                          |
| L-iditol-2 dehydrogenase (23376; SEQ ID NO:388)      | P502S                                         |                          |
| Ets transcription factor PDEF (22672; SEQ ID NO:398) | P706P                                         |                          |
| hTGR (22678; SEQ ID NO:399)                          | 19142.2, bangur.seq (22621;<br>SEQ ID NO:396) |                          |
| KIAA0295(22685; SEQ ID NO:400)                       | 5566.1 Wang (23404;<br>SEQ ID NO:393)         |                          |
| Prostatic Acid Phosphatase(22655; SEQ ID NO:397)     | P712P                                         |                          |
| transglutaminase (22611; SEQ ID NO:395)              | P778P                                         | ,                        |
| HDLBP (23508; SEQ ID NO:394)                         |                                               |                          |
| CGI-69 Protein(23367; SEQ ID NO:387)                 |                                               |                          |
| KIAA0122(23383; SEQ ID NO:391)                       |                                               | Park Tark Trans          |
| TEEG                                                 |                                               |                          |

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CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 90% of prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid phosphatase showed 9.14 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is not detected in other normal tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2 bangur showed 23.25 fold over-expression in prostate tissues as compared to other

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normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 (also referred to as P553S) showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97% of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

Subsequent full-length cloning studies on P553S, using standard techniques, revealed that this clone is an incomplete spliced form of P501S. The determined cDNA sequences for four splice variants of P553S are provided in SEQ ID NO: 623-626. An amino acid sequence encoded by SEQ ID NO: 626 is provided in SEQ ID NO: 627. The cDNA sequence of SEQ ID NO: 623 was found to contain two open reading frames (ORFs). The amino acid sequences encoded by these two ORFs are provided in SEQ ID NO: 628 and 629.

#### **EXAMPLE 14**

IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS

By ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify prostate-specific antigens.

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Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatizis et al., *Proc. Natl. Acad. Sci. USA 95*:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed genes such as those for ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups: Plus (normal prostate and prostate tumor libraries, and breast cell line libraries, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (libraries from fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

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<u>Table II</u>

<u>Prostate cDNA Libraries and ESTs</u>

| Library    | # of Libraries | # of ESTs |
|------------|----------------|-----------|
| Plus       | 25             | 43,482    |
| Normal     | 11             | 18,875    |
| Tumor      | 11             | 21,769    |
| Cell lines | 3              | 2,838     |
| Minus      | 166            |           |
| Other      | 287            |           |

Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups: Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones derived from the Plus and Other group libraries only; no expression detected in the Minus group; Type 3- EST clones derived from the Plus, Minus and Other group libraries, but the number of ESTs derived from the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones derived from Plus, Minus and Other group libraries, but the number derived from the Plus group is higher than the number derived from the Minus group. This analysis identified 4,345 breast clusters (see Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

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<u>Table III</u>

<u>Prostate Cluster Summary</u>

| # of Superclusters |       | # of ESTs<br>Ordered |      |
|--------------------|-------|----------------------|------|
| 1                  |       | 688                  | 677  |
| 2                  |       | 2899                 | 2484 |
| 3                  |       | 85                   | 11   |
| 4                  | . 1   | 673                  | 0    |
|                    | Total | 4345                 | 3172 |

The EST clone inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high levels of tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA 93*:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA 94*:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

Clones with an expression ratio greater than 3 (i.e., the level in prostate tumor and normal prostate mRNA was at least three times the level in other normal tissue mRNA) were identified as prostate tumor-specific sequences (Table IV). The sequences of these clones are provided in SEQ ID NO: 401-453, with certain novel sequences shown in SEQ ID NO: 407, 413, 416-419, 422, 426, 427 and 450.

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<u>Table IV</u>

<u>Prostate-tumor Specific Clones</u>

| SEQ ID NO.   | Sequence<br>Designation | Comments                       |  |
|--------------|-------------------------|--------------------------------|--|
| 401          | 22545                   | previously identified P1000C   |  |
| 402          | 22547                   | previously identified P704P    |  |
| 403          | 22548                   | known                          |  |
| 404          | 22550                   | known                          |  |
| <b>→</b> 405 | 22551                   | PSA                            |  |
| 406          | 22552                   | prostate secretory protein 94  |  |
| 407          | 22553                   | novel                          |  |
| 408          | 22558                   | previously identified P509S    |  |
| 409          | 22562                   | glandular kallikrein           |  |
| 410          | 22565                   | previously identified P1000C   |  |
| . 411        | 22567                   | PAP                            |  |
| 412          | 22568                   | B1006C (breast tumor antigen)  |  |
| 413          | 22570                   | novel                          |  |
| 414          | 22571                   | PSA                            |  |
| 415          | 22572                   | previously identified P706P    |  |
| 416          | 22573                   | novel                          |  |
| 417          | 22574                   | novel                          |  |
| 418          | 22575                   | novel                          |  |
| 419          | 22580                   | novel                          |  |
| 420          | 22581                   | PAP                            |  |
| 421          | 22582                   | prostatic secretory protein 94 |  |
| 422          | 22583                   | novel                          |  |
| 423          | 22584                   | prostatic secretory protein 94 |  |
| 424          | 22585                   | prostatic secretory protein 94 |  |
| 425          | 22586                   | known                          |  |
| 426          | 22587                   | novel                          |  |
| 427          | 22588                   | novel                          |  |
| 428          | 22589                   | PAP                            |  |
| 429          | 22590                   | known                          |  |
| 430          | 22591                   | PSA.                           |  |
| 431          | 22592                   | known                          |  |
| 432          | 22593                   | Previously identified P777P    |  |
| 433          | 22594                   | T cell receptor gamma chain    |  |
| 434          | 22595                   | Previously identified P705P    |  |
| 435          | 22596                   | Previously identified P707P    |  |
| 436          | 22847                   | PAP                            |  |
| 437          | 22848                   | known                          |  |
| 438          | 22849                   | prostatic secretory protein 57 |  |

| 439 | 22851   | PAP                          |  |
|-----|---------|------------------------------|--|
| 440 | 22852   | PAP                          |  |
| 441 | 22853   | PAP                          |  |
| 442 | 22854   | previously identified P509S  |  |
| 443 | 22855   | previously identified P705P  |  |
| 444 | 22856   | previously identified P774P  |  |
| 445 | - 22857 | PSA                          |  |
| 446 | 23601   | previously identified P777P  |  |
| 447 | 23602   | PSA                          |  |
| 448 | 23605   | PSA                          |  |
| 449 | 23606   | PSA                          |  |
| 450 | 23612   | novel                        |  |
| 451 | 23614   | PSA                          |  |
| 452 | 23618   | previously identified P1000C |  |
| 453 | 23622   | previously identified P705P  |  |
|     |         |                              |  |

Further studies on the clone of SEQ ID NO: 407 (also referred to as P1020C) led to the isolation of an extended cDNA sequence provided in SEQ ID NO: 591. This extended cDNA sequence was found to contain an open reading frame that encodes the predicted amino acid sequence of SEQ ID NO: 592. The P1020C cDNA and amino acid sequences were found to show some similarity to the human endogenous retroviral HERV-K pol gene and protein.

#### **EXAMPLE 15**

FURTHER IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of additional prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three 15 fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NO: 454-467. Of these sequences, SEQ ID NO: 459-460 represent novel genes. The others (SEQ ID NO: 454-458 and 461-467) correspond to known sequences. Comparison of the determined

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cDNA sequence of SEQ ID NO: 461 with sequences in the Genbank database using the BLAST program revealed homology to the previously identified transmembrane protease serine 2 (TMPRSS2). The full-length cDNA sequence for this clone is provided in SEQ ID NO: 751, with the corresponding amino acid sequence being provided in SEQ ID NO: 752. The cDNA sequence encoding the first 209 amino acids of TMPRSS2 is provided in SEQ ID NO: 753, with the first 209 amino acids being provided in SEQ ID NO: 754.

The sequence of SEQ ID NO: 462 (referred to as P835P) was found to correspond to the previously identified clone FLJ13518 (Accession AK023643; SEQ ID NO: 774), which had no associated open reading frame (ORF). This clone was used to search the Geneseq DNA database and matched a clone previously identified as a G protein-coupled receptor protein (DNA Geneseq Accession A09351; amino acid Genesed Accession Y92365), that is characterized by the presence of seven transmembrane domains. The sequences of fragments between these domains are provided in SEQ ID NO: 778-785, with SEQ ID NO: 778, 780, 782 and 784 representing extracellular domains and SEQ ID NO: 779, 781, 783 and 785 representing intracellular domains. SEQ ID NO: 778-785 represent amino acids 1-28, 53-61, 83-103, 124-143, 165-201, 226-238, 263-272 and 297-381, respectively, of P835P. The full-length cDNA sequence for P835P is provided in SEQ ID NO: 773. The cDNA sequence of the open reading frame for P835P, including stop codon, is provided in SEQ ID NO: 775, with the open reading frame without stop codon being provided in SEQ ID NO: 776 and the corresponding amino acid sequence being provided in SEQ ID NO: 777.

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# EXAMPLE 16

FURTHER CHARACTERIZATION OF PROSTATE-SPECIFIC ANTIGEN P710P

This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P 30 fragment described above. One million colonies were plated on LB/Ampicillin plates.

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Nylon membrane filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic Perkin Elmer/Applied Biosystems Division Sequencer. Four sequences were obtained, and are presented in SEQ ID NO: 468-471. These sequences appear to represent different splice variants of the P710P gene. Subsequent comparison of the cDNA sequences of P710P with those in Genbank revealed homology to the DD3 gene (Genbank accession numbers AF103907 & AF103908). The cDNA sequence of DD3 is provided in SEQ ID NO: 618.

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# PROTEIN EXPRESSION OF PROSTATE-SPECIFIC ANTIGENS

This example describes the expression and purification of prostatespecific antigens in *E. coli*, baculovirus, mammalian and yeast cells.

## a) Expression of P501S in E. coli

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Expression of the full-length form of P501S was attempted by first cloning P501S without the leader sequence (amino acids 36-553 of SEQ ID NO: 113) downstream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) in pET17b. Specifically, P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW003 (SEQ ID NO: 486). AW025 is a sense cloning primer that contains a HindIII site. AW003 is an antisense cloning primer that contains an EcoRI site. DNA amplification was performed using 5 μl 10X Pfu buffer, 1 μl 20 mM dNTPs, 1 μl each of the PCR primers at 10 μM concentration, 40 μl water, 1 μl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 μl DNA at 100 ng/μl. Denaturation at 95°C was performed for 30 sec, followed by 10 cycles of 95°C for 30 sec, 60°C for 1 min and by 72°C for 3 min, 20 cycles of 95°C for 30 sec, 65°C for 1 min and by 72°C for 3 min, and lastly by 1 cycle of 72°C for 10 min. The PCR product was

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cloned to Ra12m/pET17b using HindIII and EcoRI. The sequence of the resulting fusion construct (referred to as Ra12-P501S-F) was confirmed by DNA sequencing.

The fusion construct was transformed into BL21(DE3)pLysE, pLysS and CodonPlus E. coli (Stratagene) and grown overnight in LB broth with kanamycin. The resulting culture was induced with IPTG. Protein was transferred to PVDF membrane and blocked with 5% non-fat milk (in PBS-Tween buffer), washed three times and incubated with mouse anti-His tag antibody (Clontech) for 1 hour. The membrane was washed 3 times and probed with HRP-Protein A (Zymed) for 30 min. Finally, the membrane was washed 3 times and developed with ECL (Amersham). No expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage (Invitrogen).

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An N-terminal fragment of P501S (amino acids 36-325 of SEQ ID NO: 113) was cloned down-stream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 in pET17b as follows. P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW027 (SEQ ID NO: 487). AW027 is an antisense cloning primer that contains an EcoRI site and a stop codon. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The fusion construct (referred to as Ra12-P501S-N) was confirmed by DNA sequencing.

The Ra12-P501S-N fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, essentially as described above. Using Western blot analysis, protein bands were observed at the expected molecular weight of 36 kDa. Some high molecular weight bands were also observed, probably due to aggregation of the recombinant protein. No expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage.

A fusion construct comprising a C-terminal portion of P501S (amino acids 257-553 of SEQ ID NO: 113) located down-stream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) was prepared as follows. P501S

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DNA was used to perform PCR using the primers AW026 (SEQ ID NO: 488) and AW003 (SEQ ID NO: 486). AW026 is a sense cloning primer that contains a HindIII site. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The sequence for the fusion construct (referred to as Ra12-P501S-C) was confirmed.

The Ra12-P501S-C fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, as described above. A small amount of protein was detected by Western blot, with some molecular weight aggregates also being observed. Expression was also detected by Western blot when the Ra12-P501S-C fusion was used for expression in BL21CodonPlus induced by CE6 phage.

A fusion construct comprising a fragment of P501S (amino acids 36-298 of SEQ ID NO: 113) located down-stream of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 705) was prepared as follows. P501S DNA was used to perform PCR using the primers AW042 (SEQ ID NO: 706) and AW053 (SEQ ID NO: 707). AW042 is a sense cloning primer that contains a EcoRI site. AW053 is an antisense primer with stop and Xho I sites. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the EcoRI and Xho I sites. The resulting fusion construct (referred to as Ra12-P501S-E2) was expressed in B834 (DE3) pLys S *E. coli* host cells in TB media for 2 h at room temperature. Expressed protein was purified by washing the inclusion bodies and running on a Ni-NTA column. The purified protein stayed soluble in buffer containing 20 mM Tris-HCl (pH 8), 100 mM NaCl, 10 mM β-Me and 5% glycerol. The determined cDNA and amino acid sequences for the expressed fusion protein are provided in SEQ ID NO: 708 and 709, respectfully.

## 25 b) Expression of P501S in Baculovirus

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The Bac-to-Bac baculovirus expression system (BRL Life Technologies, Inc.) was used to express P501S protein in insect cells. Full-length P501S (SEQ ID NO: 113) was amplified by PCR and cloned into the XbaI site of the donor plasmid pFastBacI. The recombinant bacmid and baculovirus were prepared according to the

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manufacturer's instructions. The recombinant baculovirus was amplified in Sf9 cells and the high titer viral stocks were utilized to infect High Five cells (Invitrogen) to make the recombinant protein. The identity of the full-length protein was confirmed by N-terminal sequencing of the recombinant protein and by Western blot analysis (Figure 7). Specifically, 0.6 million High Five cells in 6-well plates were infected with either the unrelated control virus BV/ECD\_PD (lane 2), with recombinant baculovirus for P501S at different amounts or MOIs (lanes 4-8), or were uninfected (lane 3). Cell lysates were run on SDS-PAGE under reducing conditions and analyzed by Western blot with the anti-P501S monoclonal antibody P501S-10E3-G4D3 (prepared as described below). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

The localization of recombinant P501S in the insect cells was investigated as follows. The insect cells overexpressing P501S were fractionated into fractions of nucleus, mitochondria, membrane and cytosol. Equal amounts of protein from each fraction were analyzed by Western blot with a monoclonal antibody against P501S. Due to the scheme of fractionation, both nucleus and mitochondria fractions contain some plasma membrane components. However, the membrane fraction is basically free from mitochondria and nucleus. P501S was found to be present in all fractions that contain the membrane component, suggesting that P501S may be associated with plasma membrane of the insect cells expressing the recombinant protein.

#### c) Expression of P501S in Mammalian Cells

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Full-length P501S (553 amino acids; SEQ ID NO: 113) was cloned into various mammalian expression vectors, including pCEP4 (Invitrogen), pVR1012 (Vical, San Diego, CA) and a modified form of the retroviral vector pBMN, referred to as pBIB. Transfection of P501S/pCEP4 and P501S/pVR1012 into HEK293 fibroblasts was carried out using the Fugene transfection reagent (Boehringer Mannheim). Briefly, 2 ul of Fugene reagent was diluted into 100 ul of serum-free media and incubated at room temperature for 5-10 min. This mixture was added to 1 ug of P501S plasmid DNA, mixed briefly and incubated for 30 minutes at room temperature. The

Fugene/DNA mixture was added to cells and incubated for 24-48 hours. Expression of recombinant P501S in transfected HEK293 fibroblasts was detected by means of Western blot employing a monoclonal antibody to P501S.

Transfection of p501S/pCEP4 into CHO-K cells (American Type Culture Collection, Rockville, MD) was carried out using GenePorter transfection reagent (Gene Therapy Systems, San Diego, CA). Briefly, 15 µl of GenePorter was diluted in 500 µl of serum-free media and incubated at room temperature for 10 min. The GenePorter/media mixture was added to 2 µg of plasmid DNA that was diluted in 500 µl of serum-free media, mixed briefly and incubated for 30 min at room temperature. CHO-K cells were rinsed in PBS to remove serum proteins, and the GenePorter/DNA mix was added and incubated for 5 hours. The transfected cells were then fed an equal volume of 2x media and incubated for 24-48 hours.

FACS analysis of P501S transiently infected CHO-K cells, demonstrated surface expression of P501S. Expression was detected using rabbit polyclonal antisera raised against a P501S peptide, as described below. Flow cytometric analysis was performed using a FaCScan (Becton Dickinson), and the data were analyzed using the Cell Quest program.

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### d) Expression of P501S in S. cerevisiae

P501S was expressed in yeast, directed in membranes, using the yeast α prepro signal sequence. The natural signal sequence and first lumenal domain of P501S was deleted in order to conserve the natural positioning of the expressed P501S protein.

Specifically, the  $\alpha$  prepro signal sequence of *S. cerevisiae* linked to amino acids 55-553 of SEQ ID NO: 113 with a His tag tail was cloned into the plasmid pRIT15068 with the CUP1 promoter and transfected into *S. cerevisiae* strain Y1790. The Y1790 strain is Leu+ and His-. Expression of protein was induced by addition of either 500  $\mu$ M or 250  $\mu$ M of CuSO<sub>4</sub> at 30 °C in minimal medium supplemented with histidine. Cells were harvested 24 hours after induction. Extracts were prepared by growing cells to a concentration of OD600 5.0 in 50 mM citrate phosphate buffer (pH 4.0) plus 130 mM NaCl supplemented with protease inhibitors. Cells were disrupted

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using glass beads and centrifuged for 20 min at 15,000 g. The recombinant protein was found to be 100% pellet associated.

Expression of the recombinant protein (molecular weight 63 kD) was demonstrated by Western blot analysis, using the anti-P501S monoclonal antibody 10E-D4-G3 described below. The amino acid sequence of the expressed protein is provided in SEQ ID NO: 792.

Fermentation processes for the production of the α prepro-P501S-His tag recombinant protein in S. cerevisiae (strain Y1790 – CUP1 inducible promoter) were evaluated as follows. One hundred μl of a master seed containing 2.5 x 10<sup>8</sup> cells/ml of transformed S. cerevisiae Y1790 were spread on FSC004AA solid medium. The composition of the FSC004AA medium is as follows: glucose 10 g/l; Na<sub>2</sub>MoO<sub>4</sub>.2H<sub>2</sub>O 0.0002 g/l; folic acid 0.000064 g/l; KH<sub>2</sub>PO<sub>4</sub> 1 g/l; MnSO<sub>4</sub>.H<sub>2</sub>O 0.0004 g/l; Inositol 0.064 g/l; MgSO<sub>4</sub>.7H<sub>2</sub>O 0.5 g/l; H<sub>3</sub>BO<sub>3</sub> 0.0005 g/l; Pyridoxine 0.008 g/l; CaCl<sub>2</sub>.2H<sub>2</sub>O 0.1 g/l; KI 0.0001 g/l; Thiamine 0.008 g/l; NaCl 0.1 g/l; CoCl<sub>2</sub>.6H<sub>2</sub>O 0.00009 g/l; Niacin 0.000032 g/l; FeCl<sub>3</sub>.6H<sub>2</sub>O 0.0002 g/l; Riboflavin 0.000016 g/l; Panthotenate Ca 0.008 g/l; CuSO<sub>4</sub>.5H<sub>2</sub>O 0.00004 g/l; Biotin 0.000064 g/l; para-aminobenzoic acid 0.000016 g/l; ZnSO<sub>4</sub>.7H<sub>2</sub>O 0.00004 g/l; (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> 5 g/l; agar 18 g/l; Histidine 0.1 g/l.

Two plates were incubated for 26 h at 30 °C. These solid pre-cultures were harvested in 5 ml of liquid medium FSC007AA and 0.5 ml (or  $9.3 \times 10^7$  cells) of this suspension was used to inoculate 2 liquid pre-cultures.

The composition of the FSC007AA medium is as follows: Glucose 10 g/l; Na<sub>2</sub>MoO<sub>4</sub>.2H<sub>2</sub>O 0.0002 g/l; folic acid 0.000064 g/l; KH<sub>2</sub>PO<sub>4</sub> 1 g/l; MnSO<sub>4</sub>.H<sub>2</sub>O 0.0004 g/l; Inositol 0.064 g/l; MgSO<sub>4</sub>.7H<sub>2</sub>O 0.5 g/l; H<sub>3</sub>BO<sub>3</sub> 0.0005 g/l; Pyridoxine 0.008 g/l; CaCl<sub>2</sub>.2H<sub>2</sub>O 0.1 g/l; KI 0.0001 g/l; Thiamine 0.008 g/l; NaCl 0.1 g/l; CoCl<sub>2</sub>.6H<sub>2</sub>O 0.00009 g/l; Niacine 0.000032 g/l; FeCl<sub>3</sub>.6H<sub>2</sub>O 0.0002 g/l; Riboflavin 0.000016 g/l; Panthotenate Ca 0.008 g/l; CuSO<sub>4</sub>.5H<sub>2</sub>O 0.00004 g/l; Biotin 0.000064 g/l; para-aminobenzoic acid 0.000016 g/l; ZnSO<sub>4</sub>.7H<sub>2</sub>O 0.00004 g/l; (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> 5 g/l; Histidine 0.1 g/l.

These pre-cultures were run for 20 hours in 2L flasks containing 400 ml of medium FSC007AA in order to obtain an OD of 1.8. The other characteristics of these pre-cultures are as follows: pH 2.8; glucose 2.3 g/L; ethanol 3.4 g/L.

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The best timing for liquid pre-cultures for strain Y1790 was determined in preliminary experiments. Liquid pre-cultures containing 400 ml of medium and inoculated with various volumes of Master Seed (0.25, 0.5, 1 or 2 ml) were monitored in order to identify the best inoculum size and timing. Glucose, ethanol, pH, OD and cell number (determined by flow cytometry) were followed between 16 and 23 hours of culture. Glucose exhaustion and maximal biomass were obtained after 20 hour incubation with 0.5 inoculum. These conditions were adopted for transferring the pre-culture into fermentation.

In total, 800ml of pre-culture were used to inoculate a 20 L fermenter containing 5L of medium FSC002AA. Three ml of irradiated antifoam were added before inoculation. The composition of the FSC002AA medium is as follows: (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub> 6.4 g/l; Na<sub>2</sub>MoO<sub>4</sub>.2H<sub>2</sub>O 2.05 mg/l; folic acid 0.54 mg/l; KH<sub>2</sub>PO<sub>4</sub> 8.25 g/l; MnSO<sub>4</sub>.H<sub>2</sub>O 4.1 mg/l; inositol 540 mg/; MgSO<sub>4</sub>.7H<sub>2</sub>O 4.69 g/l; H<sub>3</sub>BO<sub>3</sub> 5.17 m/l; pyridoxine 68 mg/l; CaCl<sub>2</sub>.2H<sub>2</sub>O 0.92 g/l; KI 1.03 mg/l; thiamine 68 mg/l; NaCl 0.06g/l; CoCl<sub>2</sub>.6H<sub>2</sub>O 0.92 mg/l; Niacine 0.27 mg/l; HCl 1 ml/l; FeCl<sub>3</sub>.6H<sub>2</sub>O 9.92 mg/l; Riboflavin 0.13 mg/l; CuSO<sub>4</sub>.5H<sub>2</sub>O 0.41 mg/l; Glucose 0.14 g/l; Panthotenate Ca 68 mg/l; ZnSO<sub>4</sub>.7H<sub>2</sub>O 4.1 mg/l; Biotin 0.54 mg/l; para-aminobenzoic acid 0.13 mg/l; Histidine 0.3 g/l

The carbon source (glucose) was supplemented by a continuous feeding of FFB004AA medium. The composition of the FFB004AA medium is as follows: glucose 350 g/l; Na<sub>2</sub>MoO<sub>4</sub>.2H<sub>2</sub>O 5.15 mg/l; folic acid 1.36 mg/l; KH<sub>2</sub>PO<sub>4</sub> 20.6 g/l; MnSO<sub>4</sub>.H<sub>2</sub>O 10.3 mg/l; inositol 1350 mg/l; MgSO<sub>4</sub>.7H<sub>2</sub>O 11.7 g/l; H<sub>3</sub>BO<sub>3</sub> 12.9 m/l; pyridoxine 170 mg/l; CaCl<sub>2</sub>.2H<sub>2</sub>O 2.35 g/l; KI 2.6 mg/l; thiamine 170 g/l; NaCl 0.15 g/l; CoCl<sub>2</sub>.6H<sub>2</sub>O 2.3 mg/l; niacine 0.67 mg/l; HCl 2.5 ml/l; FeCl<sub>3</sub>.6H<sub>2</sub>O 24.8 mg/l; riboflavin; 0.33 mg/l; CuSO<sub>4</sub>.5H<sub>2</sub>O 1.03 mg/l; biotin 1.36 mg/l; panthotenate Ca 170 mg/l; ZnSO<sub>4</sub>.7H<sub>2</sub>O 10.3 mg/l; para-aminobenzoic acid: 0.33 mg/l; histidine 5.35 g/l.

The residual glucose concentration was maintained very low (\$\square\$50 mg/L) in order to minimize ethanol production by fermentation. This was achieved by limiting the development of the microorganism using a limited glucose feed rate. The Standard biomass content (OD 80-90) was reached in fermentation after 44 hour growth phase.

CUP1 promoter was then induced by adding 500µM CuSO4 in order to

produce P501S antigen. CuSO<sub>4</sub> addition was followed by ethanol accumulation (up to 6 g/L), and the glucose feeding rate was then reduced in order to consume the ethanol. The copper available for the microorganism was monitored by testing Cu ion concentration in the broth supernatant using a spectrophotometric copper assay (DETC method). The fermentation was then supplemented by CuSO<sub>4</sub> throughout the induction phase in order to maintain its concentration between 150 and 250 µM in the supernatant. The biomass reached an OD of 100 at the end of induction. Cells were harvested after 8 hours of induction.

Cell homogenate was prepared and analysed by SDS-PAGE and Western Blot using standard protocols. A major protein band with the expected molecular weight of 62KD was detected by Western blot using anti-P501S monoclonal antibodies. Western blot analysis also showed that the major 62KD band was progressively produced from 30 minutes of induction on, and reached a maximum after 3 hours. No more antigen seemed to be produced between 3 and 12 hours of induction.

The number of passages through a French Press necessary to extract all the antigen from the cells was evaluated. One, three and five passages were tested and total cell lysates, supernatants and pellets of cell lysates were analysed by Western blot. Three passages through a French Press were sufficient to completely extract the antigen. The antigen was present in the insoluble fraction.

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#### e) Expression of P703P in Baculovirus

The cDNA for full-length P703P-DE5 (SEQ ID NO: 326), together with several flanking restriction sites, was obtained by digesting the plasmid pCDNA703 with restriction endonucleases Xba I and Hind III. The resulting restriction fragment (approx. 800 base pairs) was ligated into the transfer plasmid pFastBacI which was digested with the same restriction enzymes. The sequence of the insert was confirmed by DNA sequencing. The recombinant transfer plasmid pFBP703 was used to make recombinant bacmid DNA and baculovirus using the Bac-To-Bac Baculovirus expression system (BRL Life Technologies). High Five cells were infected with the recombinant virus BVP703, as described above, to obtain recombinant P703P protein.

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# e) Expression of P788P in E. Coli

A truncated, N-terminal portion, of P788P (residues 1-644 of SEQ ID NO: 777; referred to as P788P-N) fused with a C-terminal 6xHis Tag was expressed in E. coli as follows. P788P cDNA was amplified using the primers AW080 and AW081 (SEQ ID NO: 672 and 673). AW080 is a sense cloning primer with an NdeI site. AW081 is an antisense cloning primer with a XhoI site. The PCR-amplified P788P, as well as the vector pCRX1, were digested with NdeI and XhoI. Vector and insert were ligated and transformed into NovaBlue cells. Colonies were randomly screened for insert and then sequenced. P788P-N clone #6 was confirmed to be identical to the 10 designed construct. The expression construct P788P-N #6/pCRX1 was transformed into E. coli BL21 CodonPlus-RIL competent cells. After induction, most of the cells grew well, achieving OD600 of greater than 2.0 after 3 hr. Coomassie stained SDS-PAGE showed an over-expressed band at about 75 kD. Western blot analysis using a 6xHisTag antibody confirmed the band was P788P-N. The determined cDNA sequence for P788P-N is provided in SEQ ID NO: 674, with the corresponding amino acid 15 sequence being provided in SEQ ID NO: 675.

# f) Expression of P510S in E. Coli

The P510S protein has 9 potential transmembrane domains and is predicted to be located at the plasma membrane. The C-terminal protein of this protein, as well as the predicted third extracellular domain of P510S were expressed in E. coli as follows.

The expression construct referred to as Ra12-P501S-C was designed to have a 6 HisTag at the N-terminal enc, followed by the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 676) and then the C-terminal portion of P510S (amino residues 1176-1261 of SEQ ID NO: 538). Full-length P510S was used to amplify the P510S-C fragment by PCR using the primers AW056 and AW057 (SEQ ID NO: 677 and 678, respectively). AW056 is a sense cloning primer with an EcoRI site. AW057 is an antisense primer with stop and XhoI sites. The amplified P501S fragment and Ra12/pCRX1 were digested with EcoRI and XhoI and then purified. The insert and

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vector were ligated together and transformed into NovaBlue. Colonies were randomly screened for insert and sequences. For protein expression, the expression construct was transformed into *E. coli* BL21 (DE3) CodonPlus-RIL competent cells. A minimulation screen was performed to optimize the expression conditions. After induction the cells grew well, achieving OD 600 nm greater than 2.0 after 3 hours. Coomassie stain SDS-PAGE showed a highly over-expressed band at approx. 30 kD. Though this is higher than the expected molecular weight, western blot analysis was positive, showing this band to be the His tag-containing protein. The optimized culture conditions are as follows. Dilute overnight culture/daytime culture (LB + kanamycin + chloramphenicol) into 2xYT (with kanamycin and chloramphenicol) at a ratio of 25 ml culture to 1 liter 2xYT. Allow to grow at 37 °C until OD600 = 0.6. Take an aliquot out as T0 sample. Add 1 mM IPTG and allow to grow at 30 °C for 3 hours. Take out a T3 sample, spin down cells and store at -80 °C. The determined cDNA and amino acid sequences for the Ra12-P510S-C construct are provided in SEQ ID NO: 679 and 682, respectively.

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The expression construct P510S-C was designed to have a 5' added start codon and a glycine (GGA) codon and then the P510S C terminal fragment followed by the in frame 6x histidine tag and stop codon from the pET28b vector. The cloning strategy is similar to that used for Ra12-P510S-C, except that the PCR primers employed were those shown in SEQ ID NO: 685 and 686, respectively and the NcoI/XhoI cut in pET28b was used. The primer of SEQ ID NO: 685 created a 5' NcoI site and added a start codon. The antisense primer of SEQ ID NO: 686 creates a XhoI site on P510S C terminal fragment. Clones were confirmed by sequencing. For protein expression, the expression construct was transformed into E. coli BL21 (DE3) CodonPlus-RIL competent cells. An OD600 of greater than 2.0 was obtained 30 hours after induction. Coomassie stained SDS-PAGE showed an over-expressed band at about 11 kD. Western blot analysis confirmed that the band was P510S-C, as did N-terminal protein The optimized culture conditions are as follows: dilute overnight sequencing. culture/daytime culture (LB + kanamycin + chloramphenicol) into 2x YT (+ kanamycin and chloramphenicol) at a ratio of 25 mL culture to 1 liter 2x YT, and allow to grow at

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37 °C until an OD 600 of about 0.5 is reached. Take out an aliquot as T0 sample. Add 1 mM IPTG and allow to grow at 30 °C for 3 hours. Spin down the cells and store at -80 °C until purification. The determined cDNA and amino acid sequences for the P510S-C construct are shown in SEQ ID NO: 680 and 683, respectively.

The predicted third extracellular domain of P510S (P510S-E3; residues 328-676 of SEQ ID NO: 538) was expressed in E. coli as follows. The P510S fragment was amplified by PCR using the primers shown in SEQ ID NO: 687 and 688. The primer of SEQ ID NO: 687 is a sense primer with an NdeI site for use in ligating into pPDM. The primer of SEQ ID NO: 688 is an antisense primer with an added XhoI site for use in ligating into pPDM. The resulting fragment was cloned to pPDM at the NdeI and XhoI sites. Clones were confirmed by sequencing. For protein expression, the clone ws transformed into E. coli BL21 (DE3) CodonPlus-RIL competent cells. After induction, an OD600 of greater than 2.0 was achieved after 3 hours. Coomassie stained SDS-PAGE showed an over-expressed band at about 39 kD, and N-terminal sequencing confirmed the N-terminal to be that of P510S-E3. Optimized culture conditions are as follows: dilute overnight culture/daytime culture (LB + kanamycin + chloramphenicol) into 2x YT (kanamycin and chloramphenicol) at a ratio of 25 ml culture to 1 liter 2x YT. Allow to grow at 37 °C until OD 600 equals 0.6. Take out an aliquot as T0 sample. Add 1 mM IPTG and allow to grow at 30 °C for 3 hours. Take out a T3 sample, spin down the cells and store at -80 °C until purification. The determined cDNA and amino acid sequences for the P501S-E3 construct are provided in SEQ ID NO: 681 and 684, respectively.

## g) Expression of P775S in E. Coli

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The antigen P775P contains multiple open reading frames (ORF). The third ORF, encoding the protein of SEQ ID NO: 483, has the best emotif score. An expression fusion construct containing the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 676) and P775P-ORF3 with an N-terminal 6x HisTag was prepared as follows. P775P-ORF3 was amplified using the sense PCR primers of SEQ ID NO: 689 and the antisense PCR primer of SEQ ID NO: 690. The PCR amplified fragment of P775P and

Ra12/pCRX1 were digested with the restriction enzymes EcoRI and XhoI. Vector and insert were ligated and then transformed into NovaBlue cells. Colonies were randomly screened for insert and then sequenced. A clone having the desired sequence was transformed into *E. coli* BL21 (DE3) CodonPlus-RIL competent cells. Two hours after induction, the cell density peaked at OD600 of approximately 1.8. Coomassie stained SDS-PAGE showed an over-expressed band at about 31 kD. Western blot using 6x HisTag antibody confirmed that the band was Ra12-P775P-ORF3. The determined cDNA and amino acid sequences for the fusion construct are provided in SEQ ID NO: 691 and 692, respectively.

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## H) Expression of a P703P His tag fusion protein in E. coli

The cDNA for the coding region of P703P was prepared by PCR using the primers of SEQ ID NO: 693 and 694. The PCR product was digested with EcoRI restriction enzyme, gel purified and cloned into a modified pET28 vector with a His tag in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into E. coli BL21 (DE3) pLys S expression host cells. The determined amino acid and cDNA sequences for the expressed recombinant P703P are provided in SEQ ID NO: 695 and 696, respectively.

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## I) Expression of a P705P His tag fusion protein in E. coli

The cDNA for the coding region of P705P was prepared by PCR using the primers of SEQ ID NO: 697 and 698. The PCR product was digested with EcoRI restriction enzyme, gel purified and cloned into a modified pET28 vector with a His tag in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into E. coli BL21 (DE3) pLys S and BL21 (DE3) CodonPlus expression host cells. The determined amino acid and cDNA sequences for the expressed recombinant P705P are provided in SEQ ID NO: 699 and 700, respectively.

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## J) EXPRESSION OF A P711P HIS TAG FUSION PROTEIN IN E. COLI

The cDNA for the coding region of P711P was prepared by PCR using the primers of SEQ ID NO: 701 and 702. The PCR product was digested with EcoRI restriction enzyme, gel purified and cloned into a modified pET28 vector with a His tag in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into E. coli BL21 (DE3) pLys S and BL21 (DE3) CodonPlus expression host cells. The determined amino acid and cDNA sequences for the expressed recombinant P711P are provided in SEQ ID NO: 703 and 704, respectively.

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#### EXAMPLE 18

# PREPARATION AND CHARACTERIZATION OF ANTIBODIES AGAINST PROSTATE-SPECIFIC POLYPEPTIDES

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# a) Preparation and Characterization of Polyclonal Antibodies against P703P, P504S and P509S

Polyclonal antibodies against P703P, P504S and P509S were prepared as follows.

Each prostate tumor antigen expressed in an *E. coli* recombinant expression system was grown overnight in LB broth with the appropriate antibiotics at 37°C in a shaking incubator. The next morning, 10 ml of the overnight culture was added to 500 ml to 2x YT plus appropriate antibiotics in a 2L-baffled Erlenmeyer flask. When the Optical Density (at 560 nm) of the culture reached 0.4-0.6, the cells were induced with IPTG (1 mM). Four hours after induction with IPTG, the cells were harvested by centrifugation. The cells were then washed with phosphate buffered saline and centrifuged again. The supernatant was discarded and the cells were either frozen for future use or immediately processed. Twenty ml of lysis buffer was added to the cell pellets and vortexed. To break open the *E. coli* cells, this mixture was then run

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through the French Press at a pressure of 16,000 psi. The cells were then centrifuged again and the supernatant and pellet were checked by SDS-PAGE for the partitioning of the recombinant protein. For proteins that localized to the cell pellet, the pellet was resuspended in 10 mM Tris pH 8.0, 1% CHAPS and the inclusion body pellet was washed and centrifuged again. This procedure was repeated twice more. The washed inclusion body pellet was solubilized with either 8 M urea or 6 M guanidine HCl containing 10 mM Tris pH 8.0 plus 10 mM imidazole. The solubilized protein was added to 5 ml of nickel-chelate resin (Qiagen) and incubated for 45 min to 1 hour at room temperature with continuous agitation. After incubation, the resin and protein mixture were poured through a disposable column and the flow through was collected. The column was then washed with 10-20 column volumes of the solubilization buffer. The antigen was then eluted from the column using 8M urea, 10 mM Tris pH 8.0 and 300 mM imidazole and collected in 3 ml fractions. A SDS-PAGE gel was run to determine which fractions to pool for further purification.

As a final purification step, a strong anion exchange resin such as HiPrepQ (Biorad) was equilibrated with the appropriate buffer and the pooled fractions from above were loaded onto the column. Each antigen was eluted off the column with a increasing salt gradient. Fractions were collected as the column was run and another SDS-PAGE gel was run to determine which fractions from the column to pool. The pooled fractions were dialyzed against 10 mM Tris pH 8.0. The proteins were then vialed after filtration through a 0.22 micron filter and the antigens were frozen until needed for immunization.

Four hundred micrograms of each prostate antigen was combined with 100 micrograms of muramyldipeptide (MDP). Every four weeks rabbits were boosted with 100 micrograms mixed with an equal volume of Incomplete Freund's Adjuvant (IFA). Seven days following each boost, the animal was bled. Sera was generated by incubating the blood at 4°C for 12-4 hours followed by centrifugation.

Ninety-six well plates were coated with antigen by incubating with 50 microliters (typically 1 microgram) of recombinant protein at 4 °C for 20 hours. 250 microliters of BSA blocking buffer was added to the wells and incubated at room

temperature for 2 hours. Plates were washed 6 times with PBS/0.01% Tween. Rabbit sera was diluted in PBS. Fifty microliters of diluted sera was added to each well and incubated at room temperature for 30 min. Plates were washed as described above before 50 microliters of goat anti-rabbit horse radish peroxidase (HRP) at a 1:10000 dilution was added and incubated at room temperature for 30 min. Plates were again washed as described above and 100 microliters of TMB microwell peroxidase substrate was added to each well. Following a 15 min incubation in the dark at room temperature, the colorimetric reaction was stopped with 100 microliters of 1N H<sub>2</sub>SO<sub>4</sub> and read immediately at 450 nm. All polyclonal antibodies showed immunoreactivity to the appropriate antigen.

# b) Preparation and Characterization of Antibodies against P501S

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A murine monoclonal antibody directed against the carboxy-terminus of the prostate-specific antigen P501S was prepared as follows.

A truncated fragment of P501S (amino acids 355-526 of SEQ ID NO: 113) was generated and cloned into the pET28b vector (Novagen) and expressed in E. coli as a thioredoxin fusion protein with a histidine tag. The trx-P501S fusion protein was purified by nickel chromatography, digested with thrombin to remove the trx fragment and further purified by an acid precipitation procedure followed by reverse phase HPLC.

Mice were immunized with truncated P501S protein. Serum bleeds from mice that potentially contained anti-P501S polyclonal sera were tested for P501S-specific reactivity using ELISA assays with purified P501S and trx-P501S proteins. Serum bleeds that appeared to react specifically with P501S were then screened for P501S reactivity by Western analysis. Mice that contained a P501S-specific antibody component were sacrificed and spleen cells were used to generate anti-P501S antibody producing hybridomas using standard techniques. Hybridoma supernatants were tested for P501S-specific reactivity initially by ELISA, and subsequently by FACS analysis of reactivity with P501S transduced cells. Based on these results, a monoclonal hybridoma referred to as 10E3 was chosen for further subcloning. A number of subclones were

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generated, tested for specific reactivity to P501S using ELISA and typed for IgG isotype. The results of this analysis are shown below in Table V. Of the 16 subclones tested, the monoclonal antibody 10E3-G4-D3 was selected for further study.

Table V

Isotype analysis of murine anti-P501S monoclonal antibodies

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| -Hybridoma clone | Isotype | Estimated [Ig] in supernatant (µġ/ml) |  |  |
|------------------|---------|---------------------------------------|--|--|
| 4D11             | IgG1    | 14.6                                  |  |  |
| 1G1,             | IgG1    | 0.6                                   |  |  |
| 4F6              | IgG1    | 72                                    |  |  |
| 4H5              | IgG1    | 13.8                                  |  |  |
| 4H5-E12          | IgG1    | 10.7                                  |  |  |
| 4H5-EH2          | IgG1    | <b>9.2</b>                            |  |  |
| 4H5-H2-A10       | IgG1    | 10                                    |  |  |
| 4H5-H2-A3        | IgG1    | 12.8                                  |  |  |
| 4H5-H2-A10-G6    | IgG1    | 13.6                                  |  |  |
| 4H5-H2-B11       | IgG1    | 12.3                                  |  |  |
| 10E3             | IgG2a   | 3.4                                   |  |  |
| 10E3-D4          | IgG2a   | 3.8                                   |  |  |
| 10E3-D4-G3       | IgG2a   | 9.5                                   |  |  |
| 10E3-D4-G6       | IgG2a   | 10.4                                  |  |  |
| 10E3-E7          | IgG2a   | 6.5                                   |  |  |
| 8H12             | IgG2a   | 0.6                                   |  |  |

The specificity of 10E3-G4-D3 for P501S was examined by FACS analysis. Specifically, cells were fixed (2% formaldehyde, 10 minutes), permeabilized (0.1% saponin, 10 minutes) and stained with 10E3-G4-D3 at 0.5 – 1 μg/ml, followed by incubation with a secondary, FITC-conjugated goat anti-mouse Ig antibody (Pharmingen, San Diego, CA). Cells were then analyzed for FITC fluorescence using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. For analysis of infected cells, B-LCL were infected with a vaccinia vector that expresses P501S. To demonstrate specificity in these assays, B-LCL transduced with a different antigen (P703P) and uninfected B-LCL vectors were utilized. 10E3-G4-D3 was shown to bind with P501S-transduced B-

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LCL and also with P501S-infected B-LCL, but not with either uninfected cells or P703P-transduced cells.

To determine whether the epitope recognized by 10E3-G4-D3 was found on the surface or in an intracellular compartment of cells, B-LCL were transduced with P501S or HLA-B8 as a control antigen and either fixed and permeabilized as described above or directly stained with 10E3-G4-D3 and analyzed as above. Specific recognition of P501S by 10E3-G4-D3 was found to require permeabilization, suggesting that the epitope recognized by this antibody is intracellular.

The reactivity of 10E3-G4-D3 with the three prostate tumor cell lines Lncap, PC-3 and DU-145, which are known to express high, medium and very low levels of P501S, respectively, was examined by permeabilizing the cells and treating them as described above. Higher reactivity of 10E3-G4-D3 was seen with Lncap than with PC-3, which in turn showed higher reactivity that DU-145. These results are in agreement with the real time PCR and demonstrate that the antibody specifically recognizes P501S in these tumor cell lines and that the epitope recognized in prostate tumor cell lines is also intracellular.

Specificity of 10E3-G4-D3 for P501S was also demonstrated by Western blot analysis. Lysates from the prostate tumor cell lines Lncap, DU-145 and PC-3, from P501S-transiently transfected HEK293 cells, and from non-transfected HEK293 cells were generated. Western blot analysis of these lysates with 10E3-G4-D3 revealed a 46 kDa immunoreactive band in Lncap, PC-3 and P501S-transfected HEK cells, but not in DU-145 cells or non-transfected HEK293 cells. P501S mRNA expression is consistent with these results since semi-quantitative PCR analysis revealed that P501S mRNA is expressed in Lncap, to a lesser but detectable level in PC-3 and not at all in DU-145 cells. Bacterially expressed and purified recombinant P501S (referred to as P501SStr2) was recognized by 10E3-G4-D3 (24 kDa), as was full-length P501S that was transiently expressed in HEK293 cells using either the expression vector VR1012 or pCEP4. Although the predicted molecular weight of P501S is 60.5 kDa, both transfected and "native" P501S run at a slightly lower mobility due to its hydrophobic nature.

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Immunohistochemical analysis was performed on prostate tumor and a panel of normal tissue sections (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). Tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with 10E3-G4-D3 antibody for 1 hr. HRP-labeled antimouse followed by incubation with DAB chromogen was used to visualize P501S immunoreactivity. P501S was found to be highly expressed in both normal prostate and prostate tumor tissue but was not detected in any of the other tissues tested.

To identify the epitope recognized by 10E3-G4-D3, an epitope mapping approach was pursued. A series of 13 overlapping 20-21 mers (5 amino acid overlap; SEQ ID NO: 489-501) was synthesized that spanned the fragment of P501S used to generate 10E3-G4-D3. Flat bottom 96 well microtiter plates were coated with either the peptides or the P501S fragment used to immunize mice, at 1 microgram/ml for 2 hours at 37 °C. Wells were then aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature, and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified antibody 10E3-G4-D3 was added at 2 fold dilutions (1000 ng - 16 ng) in PBST and incubated for 30 minutes at room temperature. This was followed by washing 6 times with PBST and subsequently incubating with HRP-conjugated donkey anti-mouse IgG (H+L)Affinipure F(ab') fragment (Jackson Immunoresearch, West Grove, PA) at 1:20000 for 30 minutes. Plates were then washed and incubated for 15 minutes in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 8, reactivity was seen with the peptide of SEQ ID NO: 496 (corresponding to amino acids 439-459 of P501S) and with the P501S fragment but not with the remaining peptides, demonstrating that the epitope recognized by 10E3-G4-D3 is localized to amino acids 439-459 of SEQ ID NO: 113.

In order to further evaluate the tissue specificity of P501S, multi-array immunohistochemical analysis was performed on approximately 4700 different human tissues encompassing all the major normal organs as well as neoplasias derived from

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these tissues. Sixty-five of these human tissue samples were of prostate origin. Tissue sections 0.6 mm in diameter were formalin-fixed and paraffin embedded. Samples were pretreated with HIER using 10 mM citrate buffer pH 6.0 and boiling for 10 min. Sections were stained with 10E3-G4-D3 and P501S immunoreactivity was visualized with HRP. All the 65 prostate tissues samples (5 normal, 55 untreated prostate tumors, 5 hormone refractory prostate tumors) were positive, showing distinct perinuclear staining. All other tissues examined were negative for P501S expression.

# c) Preparation and Characterization of Antibodies against P503S

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A fragment of P503S (amino acids 113-241 of SEQ ID NO: 114) was expressed and purified from bacteria essentially as described above for P501S and used to immunize both rabbits and mice. Mouse monoclonal antibodies were isolated using standard hybridoma technology as described above. Rabbit monoclonal antibodies were isolated using Selected Lymphocyte Antibody Method (SLAM) technology at Immgenics Pharmaceuticals (Vancouver, BC, Canada). Table VI, below, lists the monoclonal antibodies that were developed against P503S.

Table VI

| Antibody                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Species                    |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|
| 20D4                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Rabbit                     |
| JA1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Rabbit                     |
| 1A4                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Mouse                      |
| 1C3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Mouse                      |
| 1C9                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Mouse                      |
| 1 to 10 to 1 | Mouse                      |
| 2A11                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Mouse                      |
| 2H9                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Mouse                      |
| (0.33) (a) (b) (4H7) (c) (a) (a) (b) (b)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Mouse                      |
| 8A8                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Mouse                      |
| 8D10                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Mouse                      |
| 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | la the L. Mouse bedomest e |
| 6D12                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Mouse                      |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                            |

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The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 20D4 and JA1 were determined and are provided in SEQ ID NO: 502 and 503, respectively.

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In order to better define the epitope binding region of each of the antibodies, a series of overlapping peptides were generated that span amino acids 109-213 of SEO ID NO: 114. These peptides were used to epitope map the anti-P503S monoclonal antibodies by ELISA as follows. The recombinant fragment of P503S that was employed as the immunogen was used as a positive control. Ninety-six well microtiter plates were coated with either peptide or recombinant antigen at 20 ng/well overnight at 4 °C. Plates were aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature then washed in PBS containing 0.1% Tween 20 (PBST). Purified rabbit monoclonal antibodies diluted in PBST were added to the wells and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubation with Protein-A HRP conjugate at a 1:2000 dilution for a further 30 min. Plates were washed six times in PBST and incubated with tetramethylbenzidine (TMB) substrate for a further 15 min. The reaction was stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using at ELISA plate reader. ELISA with the mouse monoclonal antibodies was performed with supernatants from tissue culture run neat in the assay.

All of the antibodies bound to the recombinant P503S fragment, with the exception of the negative control SP2 supernatant. 20D4, JA1 and 1D12 bound strictly to peptide #2101 (SEQ ID NO: 504), which corresponds to amino acids 151-169 of SEQ ID NO: 114. 1C3 bound to peptide #2102 (SEQ ID NO: 505), which corresponds to amino acids 165-184 of SEQ ID NO: 114. 9C12 bound to peptide #2099 (SEQ ID NO: 522), which corresponds to amino acids 120-139 of SEQ ID NO: 114. The other antibodies bind to regions that were not examined in these studies.

Subsequent to epitope mapping, the antibodies were tested by FACS analysis on a cell line that stably expressed P503S to confirm that the antibodies bind to cell surface epitopes. Cells stably transfected with a control plasmid were employed as

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a negative control. Cells were stained live with no fixative. 0.5 ug of anti-P503S monoclonal antibody was added and cells were incubated on ice for 30 min before being washed twice and incubated with a FITC-labelled goat anti-rabbit or mouse secondary antibody for 20 min. After being washed twice, cells were analyzed with an Excalibur fluorescent activated cell sorter. The monoclonal antibodies 1C3, 1D12, 9C12, 20D4 and JA1, but not 8D3, were found to bind to a cell surface epitope of P503S.

In order to determine which tissues express P503S, immunohistochemical analysis was performed, essentially as described above, on a panel of normal tissues (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). HRPlabeled anti-mouse or anti-rabbit antibody followed by incubation with TMB was used to visualize P503S immunoreactivity. P503S was found to be highly expressed in prostate tissue, with lower levels of expression being observed in cervix, colon, ileum and kidney, and no expression being observed in adrenal, breast, duodenum, gall 15 bladder, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis.

Western blot analysis was used to characterize anti-P503S monoclonal antibody specificity. SDS-PAGE was performed on recombinant (rec) P503S expressed in and purified from bacteria and on lysates from HEK293 cells transfected with full length P503S. Protein was transferred to nitrocellulose and then Western blotted with each of the anti-P503S monoclonal antibodies (20D4, JA1, 1D12, 6D12 and 9C12) at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to either a goat anti-mouse monoclonal antibody or to protein A-sepharose. The monoclonal antibody 20D4 detected the appropriate molecular weight 14 kDa recombinant P503S (amino acids 113-241) and the 23.5 kDa species in the HEK293 cell lysates transfected with full length P503S. Other anti-P503S monoclonal antibodies displayed similar specificity by Western blot.

#### d) Preparation and Characterization of Antibodies against P703P

Rabbits were immunized with either a truncated (P703Ptr1; SEQ ID NO: 172) or full-length mature form (P703Pfl; SEQ ID NO: 523) of recombinant P703P

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protein was expressed in and purified from bacteria as described above. Affinity purified polyclonal antibody was generated using immunogen P703Pfl or P703Ptr1 attached to a solid support. Rabbit monoclonal antibodies were isolated using SLAM technology at Immgenics Pharmaceuticals. Table VII below lists both the polyclonal and monoclonal antibodies that were generated against P703P.

Table VII

| Antibody                               | Immunogen | Species/type      |
|----------------------------------------|-----------|-------------------|
| Aff. Purif. P703P (truncated); #2594   | P703Ptrl  | Rabbit polyclonal |
| Aff. Purif. P703P (full length); #9245 | P703Pfl   | Rabbit polyclonal |
| 2D4                                    | P703Ptrl  | Rabbit monoclonal |
| 8H2                                    | P703Ptrl  | Rabbit monoclonal |
| 7H8                                    | P703Ptrl  | Rabbit monoclonal |

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 8H2, 7H8 and 2D4 were determined and are provided in SEQ ID NO: 506-508, respectively.

Epitope mapping studies were performed as described above. Monoclonal antibodies 2D4 and 7H8 were found to specifically bind to the peptides of SEQ ID NO: 509 (corresponding to amino acids 145-159 of SEQ ID NO: 172) and SEQ ID NO: 510 (corresponding to amino acids 11-25 of SEQ ID NO: 172), respectively. The polyclonal antibody 2594 was found to bind to the peptides of SEQ ID NO: 511-514, with the polyclonal antibody 9427 binding to the peptides of SEQ ID NO: 515-517.

The specificity of the anti-P703P antibodies was determined by Western blot analysis as follows. SDS-PAGE was performed on (1) bacterially expressed recombinant antigen; (2) lysates of HEK293 cells and Ltk-/- cells either untransfected or transfected with a plasmid expressing full length P703P; and (3) supernatant isolated from these cell cultures. Protein was transferred to nitrocellulose and then Western blotted using the anti-P703P polyclonal antibody #2594 at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to an anti-rabbit antibody. A 35 kDa immunoreactive band could be observed with

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recombinant P703P. Recombinant P703P runs at a slightly higher molecular weight since it is epitope tagged. In lysates and supernatants from cells transfected with full length P703P, a 30 kDa band corresponding to P703P was observed. To assure specificity, lysates from HEK293 cells stably transfected with a control plasmid were also tested and were negative for P703P expression. Other anti-P703P antibodies showed similar results.

Immunohistochemical studies were performed as described above, using anti-P703P monoclonal antibody. P703P was found to be expressed at high levels in normal prostate and prostate tumor tissue but was not detectable in all other tissues tested (breast tumor, lung tumor and normal kidney).

# e) Preparation and Characterization of Antibodies against P504S

Full-length P504S (SEQ ID NO: 108) was expressed and purified from bacteria essentially as described above for P501S and employed to raise rabbit monoclonal antibodies using Selected Lymphocyte Antibody Method (SLAM) technology at Immgenics Pharmaceuticals (Vancouver, BC, Canada). The anti-P504S monoclonal antibody 13H4 was shown by Western blot to bind to both expressed recombinant P504S and to native P504S in tumor cells.

Immunohistochemical studies using 13H4 to assess P504S expression in various prostate tissues were performed as described above. A total of 104 cases, including 65 cases of radical prostatectomies with prostate cancer (PC), 26 cases of prostate biopsies and 13 cases of benign prostate hyperplasia (BPH), were stained with the anti-P504S monoclonal antibody 13H4. P504S showed strongly cytoplasmic granular staining in 64/65 (98.5%) of PCs in prostatectomies and 26/26 (100%) of PCs in prostatic biopsies. P504S was stained strongly and diffusely in carcinomas (4+ in 91.2% of cases of PC; 3+ in 5.5%; 2+ in 2.2% and 1+ in 1.1%) and high grade prostatic intraepithelial neoplasia (4+ in all cases). The expression of P504S did not vary with Gleason score. Only 17/91 (18.7%) of cases of NP/BPH around PC and 2/13 (15.4%) of BPH cases were focally (1+, no 2+ to 4+ in all cases) and weakly positive for P504S in large glands. Expression of P504S was not found in small atrophic glands, postatrophic hyperplasia, basal cell hyperplasia and transitional cell metaplasia in either biopsies or

prostatectomies. P504S was thus found to be over-expressed in all Gleason scores of prostate cancer (98.5 to 100% of sensitivity) and exhibited only focal positivities in large normal glands in 19/104 of cases (82.3% of specificity). These findings indicate that P504S may be usefully employed for the diagnosis of prostate cancer.

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#### **EXAMPLE 19**

### CHARACTERIZATION OF CELL SURFACE EXPRESSION AND

CHROMOSOME LOCALIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

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This example describes studies demonstrating that the prostate-specific antigen P501S is expressed on the surface of cells, together with studies to determine the probable chromosomal location of P501S.

The protein P501S (SEQ ID NO: 113) is predicted to have 11 transmembrane domains. Based on the discovery that the epitope recognized by the anti-P501S monoclonal antibody 10E3-G4-D3 (described above in Example 17) is intracellular, it was predicted that following transmembrane determinants would allow the prediction of extracellular domains of P501S. Fig. 9 is a schematic representation of the P501S protein showing the predicted location of the transmembrane domains and the intracellular epitope described in Example 17. Underlined sequence represents the predicted transmembrane domains, bold sequence represents the predicted extracellular domains, and italicized sequence represents the predicted intracellular domains. Sequence that is both bold and underlined represents sequence employed to generate polyclonal rabbit serum. The location of the transmembrane domains was predicted using HHMTOP as described by Tusnady and Simon (Principles Governing Amino Acid Composition of Integral Membrane Proteins: Applications to Topology Prediction, J. Mol. Biol. 283:489-506, 1998).

Based on Fig. 9, the P501S domain flanked by the transmembrane domains corresponding to amino acids 274-295 and 323-342 is predicted to be extracellular. The peptide of SEQ ID NO: 518 corresponds to amino acids 306-320 of P501S and lies in the predicted extracellular domain. The peptide of SEQ ID NO: 519,

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which is identical to the peptide of SEQ ID NO: 518 with the exception of the substitution of the histidine with an asparginine, was synthesized as described above. A Cys-Gly was added to the C-terminus of the peptide to facilitate conjugation to the carrier protein. Cleavage of the peptide from the solid support was carried out using the following cleavage mixture: trifluoroacetic acid:ethanediol:thioanisol:water:phenol (40:1:2:2:3). After cleaving for two hours, the peptide was precipitated in cold ether. The peptide pellet was then dissolved in 10% v/v acetic acid and lyophilized prior to parification by C18 reverse phase hplc. A gradient of 5-60% acetonitrile (containing 0.05% TFA) in water (containing 0.05% TFA) was used to elute the peptide. The purity of the peptide was verified by hplc and mass spectrometry, and was determined to be >95%. The purified peptide was used to generate rabbit polyclonal antisera as described above.

Surface expression of P501S was examined by FACS analysis. Cells were stained with the polyclonal anti-P501S peptide serum at 10 μg/ml, washed, incubated with a secondary FITC-conjugated goat anti-rabbit Ig antibody (ICN), washed and analyzed for FITC fluorescence using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. To demonstrate specificity in these assays, B-LCL transduced with an irrelevant antigen (P703P) or nontransduced were stained in parallel. For FACS analysis of prostate tumor cell lines, Lncap, PC-3 and DU-145 were utilized. Prostate tumor cell lines were dissociated from tissue culture plates using cell dissociation medium and stained as above. All samples were treated with propidium iodide (PI) prior to FACS analysis, and data was obtained from PI-excluding (i.e., intact and non-permeabilized) cells. The rabbit polyclonal serum generated against the peptide of SEQ ID NO: 519 was shown to specifically recognize the surface of cells transduced to express P501S, demonstrating that the epitope recognized by the polyclonal serum is extracellular.

To determine biochemically if P501S is expressed on the cell surface, peripheral membranes from Lncap cells were isolated and subjected to Western blot analysis. Specifically, Lncap cells were lysed using a dounce homogenizer in 5 ml of homogenization buffer (250 mM sucrose, 10 mM HEPES, 1mM EDTA, pH 8.0, 1

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complete protease inhibitor tablet (Boehringer Mannheim)). Lysate samples were spun at 1000 g for 5 min at 4 °C. The supernatant was then spun at 8000g for 10 min at 4 °C. Supernatant from the 8000g spin was recovered and subjected to a 100,000g spin for 30 min at 4 °C to recover peripheral membrane. Samples were then separated by SDS-PAGE and Western blotted with the mouse monoclonal antibody 10E3-G4-D3 (described above in Example 17) using conditions described above. Recombinant purified P501S, as well as HEK293 cells transfected with and over-expressing P501S were included as positive controls for P501S detection. LCL cell lysate was included as a negative control. P501S could be detected in Lncap total cell lysate, the 8000g (internal membrane) fraction and also in the 100,000g (plasma membrane) fraction. These results indicate that P501S is expressed at, and localizes to, the peripheral membrane.

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To demonstrate that the rabbit polyclonal antiserum generated to the peptide of SEQ ID NO: 519 specifically recognizes this peptide as well as the corresponding native peptide of SEQ ID NO: 518, ELISA analyses were performed. For these analyses, flat-bottomed 96 well microtiter plates were coated with either the peptide of SEQ ID NO: 519, the longer peptide of SEQ ID NO: 520 that spans the entire predicted extracellular domain, the peptide of SEQ ID NO: 521 which represents the epitope recognized by the P501S-specific antibody 10E3-G4-D3, or a P501S fragment (corresponding to amino acids 355-526 of SEQ ID NO: 113) that does not include the immunizing peptide sequence, at 1 µg/ml for 2 hours at 37 °C. Wells were aspirated, blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified anti-P501S polyclonal rabbit serum was added at 2 fold dilutions (1000 ng -125 ng) in PBST and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubating with HRP-conjugated goat anti-rabbit IgG (H+L) Affinipure F(ab') fragment at 1:20000 for 30 min. Plates were then washed and incubated for 15 min in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 11, the anti-P501S polyclonal rabbit serum specifically recognized the

peptide of SEQ ID NO: 519 used in the immunization as well as the longer peptide of SEQ ID NO: 520, but did not recognize the irrelevant P501S-derived peptides and fragments.

In further studies, rabbits were immunized with peptides derived from the P501S sequence and predicted to be either extracellular or intracellular, as shown in Fig. 9. Polyclonal rabbit sera were isolated and polyclonal antibodies in the serum were purified, as described above. To determine specific reactivity with P501S, FACS analysis was employed, utilizing either B-LCL transduced with P501S or the irrelevant antigen P703P, of B-LCL infected with vaccinia virus-expressing P501S. For surface expression, dead and non-intact cells were excluded from the analysis as described above. For intracellular staining, cells were fixed and permeabilized as described above. Rabbit polyclonal serum generated against the peptide of SEQ ID NO: 548, which corresponds to amino acids 181-198 of P501S, was found to recognize a surface epitope of P501S. Rabbit polyclonal serum generated against the peptide SEQ ID NO: 551, which corresponds to amino acids 543-553 of P501S, was found to recognize an epitope that was either potentially extracellular or intracellular since in different experiments intact or permeabilized cells were recognized by the polyclonal sera. Based on similar deductive reasoning, the sequences of SEQ ID NO: 541-547, 549 and 550, which correspond to amino acids 109-122, 539-553, 509-520, 37-54, 342-359, 295-323, 217-274, 143-160 and 75-88, respectively, of P501S, can be considered to be potential surface epitopes of P501S recognized by antibodies.

In further studies, mouse monoclonal antibodies were raised against amino acids 296 to 322 to P501S, which are predicted to be in an extracellular domain. A/J mice were immunized with P501S/adenovirus, followed by subsequent boosts with an *E. coli* recombinant protein, referred to as P501N, that contains amino acids 296 to 322 of P501S, and with peptide 296-322 (SEQ ID NO: 755) coupled with KLH. The mice were subsequently used for splenic B cell fusions to generate anti-peptide hybridomas. The resulting 3 clones, referred to as 4F4 (IgG1,kappa), 4G5 (IgG2a,kappa) and 9B9 (IgG1,kappa), were grown for antibody production. The 4G5 mAb was purified by passing the supernatant over a Protein A-sepharose column,

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followed by antibody elution using 0.2M glycine, pH 2.3. Purified antibody was neutralized by the addition of 1M Tris, pH 8, and buffer exchanged into PBS.

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For ELISA analysis, 96 well plates were coated with P501S peptide 296-322 (referred to as P501-long), an irrelevant P775 peptide, P501S-N, P501TR2, P501Slong-KLH, P501S peptide 306-319 (referred to as P501-short)-KLH, or the irrelevant peptide 2073-KLH, all at a concentration of 2 ug/ml and allowed to incubate for 60 minutes at 37 °C. After coating, plates were washed 5X with PBS + 0.1% Tween and then blocked with PBS, 0.5% BSA, 0.4% Tween20 for 2 hours at room temperature. Following the addition of supernatants or purified mAb, the plates were incubated for 60 minutes at room temperature. Plates were washed as above and donkey anti-mouse IgHRP-linked secondary antibody was added and incubated for 30 minutes at room temperature, followed by a final washing as above. TMB peroxidase substrate was added and incubated 15 minutes at room temperature in the dark. The reaction was stopped by the addition of 1N H<sub>2</sub>SO<sub>4</sub> and the OD was read at 450 nM. All three hybrid clones secreted mAb that recognized peptide 296-322 and the recombinant protein P501N.

For FACS analysis, HEK293 cells were transiently transfected with a P501S/VR1012 expression constructs using Fugene 6 reagent. After 2 days of culture, cells were harvested and washed, then incubated with purified 4G5 mAb for 30 minutes on ice. After several washes in PBS, 0.5% BSA, 0.01% azide, goat anti-mouse Ig-FITC was added to the cells and incubated for 30 minutes on ice. Cells were washed and resuspended in wash buffer including 1% propidium iodide and subjected to FACS analysis. The FACS analysis confirmed that amino acids 296-322 of P501S are in an extracellular domain and are cell surface expressed.

The chromosomal location of P501S was determined using the GeneBridge 4 Radiation Hybrid panel (Research Genetics). The PCR primers of SEQ ID NO: 528 and 529 were employed in PCR with DNA pools from the hybrid panel according to the manufacturer's directions. After 38 cycles of amplification, the reaction products were separated on a 1.2% agarose gel, and the results were analyzed 30 through the Whitehead Institute/MIT Center for Genome Research web server

(http://www-genome.wi.mit.edu/cgi-bin/contig/rhmapper.pl) to determine the probable chromosomal location. Using this approach, P501S was mapped to the long arm of chromosome 1 at WI-9641 between q32 and q42. This region of chromosome 1 has been linked to prostate cancer susceptibility in hereditary prostate cancer (Smith et al. Science 274:1371-1374, 1996 and Berthon et al. Am. J. Hum. Genet. 62:1416-1424, 1998). These results suggest that P501S may play a role in prostate cancer malignancy.

## EXAMPLE 20

### REGULATION OF EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

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Steroid (androgen) hormone modulation is a common treatment modality in prostate cancer. The expression of a number of prostate tissue-specific antigens have previously been demonstrated to respond to androgen. The responsiveness of the prostate-specific antigen P501S to androgen treatment was examined in a tissue culture system as follows.

Cells from the prostate tumor cell line LNCaP were plated at 1.5 x 10<sup>6</sup> cells/T75 flask (for RNA isolation) or 3 x 10<sup>5</sup> cells/well of a 6-well plate (for FACS analysis) and grown overnight in RPMI 1640 media containing 10% charcoal-stripped fetal calf serum (BRL Life Technologies, Gaithersburg, MD). Cell culture was continued for an additional 72 hours in RPMI 1640 media containing 10% charcoal-stripped fetal calf serum, with 1 nM of the synthetic androgen Methyltrienolone (R1881; New England Nuclear) added at various time points. Cells were then harvested for RNA isolation and FACS analysis at 0, 1, 2, 4, 8, 16, 24, 28 and 72-hours post androgen addition. FACS analysis was performed using the anti-P501S antibody 10E3-G4-D3 and permeabilized cells.

For Northern analysis, 5-10 micrograms of total RNA was run on a formaldehyde denaturing gel, transferred to Hybond-N nylon membrane (Amersham Pharmacia Biotech, Piscataway, NJ), cross-linked and stained with methylene blue. The filter was then prehybridized with Church's Buffer (250 mM Na<sub>2</sub>HPO<sub>4</sub>, 70 mM H<sub>3</sub>PO<sub>4</sub>, 1 mM EDTA, 1% SDS, 19 BSA in pH 7.2) at 65 °C for 1 hour. P501S DNA was

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labeled with 32P using High Prime random-primed DNA labeling kit (Boehringer Mannheim). Unincorporated label was removed using MicroSpin S300-HR columns (Amersham Pharmacia Biotech). The RNA filter was then hybridized with fresh Church's Buffer containing labeled cDNA overnight, washed with 1X SCP (0.1 M NaCl, 0.03 M Na<sub>2</sub>HPO<sub>4</sub>.7H<sub>2</sub>O, 0.001 M Na<sub>2</sub>EDTA), 1% sarkosyl (n-lauroylsarcosine) and exposed to X-ray film.

Using both FACS and Northern analysis, P501S message and protein levels were found in increase in response to androgen treatment.

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#### **EXAMPLE 20**

## PREPARATION OF FUSION PROTEINS OF PROSTATE-SPECIFIC ANTIGENS

The example describes the preparation of a fusion protein of the prostate-specific antigen P703P and a truncated form of the known prostate antigen PSA. The truncated form of PSA has a 21 amino acid deletion around the active serine site. The expression construct for the fusion protein also has a restriction site at 3' end, immediately prior to the termination codon, to aid in adding cDNA for additional antigens.

The full-length cDNA for PSA was obtained by RT-PCR from a pool of RNA from human prostate tumor tissues using the primers of SEQ ID NO: 607 and 608, and cloned in the vector pCR-Blunt II-TOPO. The resulting cDNA was employed as a template to make two different fragments of PSA by PCR with two sets of primers (SEQ ID NO: 609 and 610; and SEQ ID NO: 611 and 612). The PCR products having the expected size were used as templates to make truncated forms of PSA by PCR with the primers of SEQ ID NO: 611 and 613, which generated PSA (delta 208-218 in amino acids). The cDNA for the mature form of P703P with a 6X histidine tag at the 5' end, was prepared by PCR with P703P and the primers of SEQ ID NO: 614 and 615. The cDNA for the fusion of P703P with the truncated form of PSA (referred to as FOPP) was then obtained by PCR using the modified P703P cDNA and the truncated form of PSA cDNA as templates and the primers of SEQ ID NO: 614 and 615. The FOPP

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cDNA was cloned into the NdeI site and XhoI site of the expression vector pCRX1, and confirmed by DNA sequencing. The determined cDNA sequence for the fusion construct FOPP is provided in SEQ ID NO: 616, with the amino acid sequence being provided in SEQ'ID NO: 617.

The fusion FOPP was expressed as a single recombinant protein in E. coli as follows. The expression plasmid pCRX1FOPP was transformed into the E. coli strain BL21-CodonPlus RIL. The transformant was shown to express FOPP protein upon induction with 1 mM IPTG. The culture of the corresponding expression clone was inoculated into 25 ml LB broth containing 50 ug/ml kanamycin and 34 ug/ml chloramphenicol, grown at 37 °C to OD600 of about 1, and stored at 4 °C overnight. The culture was diluted into 1 liter of TB LB containing 50 ug/ml kanamycin and 34 ug/ml chloramphenicol, and grown at 37 °C to OD600 of 0.4. IPTG was added to a final concentration of 1 mM, and the culture was incubated at 30 °C for 3 hours. The cells were pelleted by centrifugation at 5,000 RPM for 8 min. To purify the protein, the cell pellet was suspended in 25 ml of 10 mM Tris-Cl pH 8.0, 2mM PMSF, complete protease inhibitor and 15 ug lysozyme. The cells were lysed at 4 °C for 30 minutes, sonicated several times and the lysate centrifuged for 30 minutes at 10,000 x g. The precipitate, which contained the inclusion body, was washed twice with 10 mM Tris-Cl pH 8.0 and 1% CHAPS. The inclusion body was dissolved in 40 ml of 10 mM Tris-Cl 20 pH 8.0, 100 mM sodium phosphate and 8 M urea. The solution was bound to 8 ml Ni-NTA (Qiagen) for one hour at room temperature. The mixture was poured into a 25 ml column and washed with 50 ml of 10 mM Tris-Cl pH 6.3, 100 mM sodium phosphate, 0.5% DOC and 8M urea. The bound protein was eluted with 350 mM imidazole, 10 mM Tris-Cl pH 8.0, 100 mM sodium phosphate and 8 M urea. The fractions containing FOPP proteins were combined and dialyzed extensively against 10 mM Tris-Cl pH 4.6, aliquoted and stored at - 70 °C.

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#### EXAMPLE 21

REAL-TIME PCR CHARACTERIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S IN
PERIPHERAL BLOOD OF PROSTATE CANCER PATIENTS

Circulating epithelial cells were isolated from fresh blood of normal individuals and metastatic prostate cancer patients, mRNA isolated and cDNA prepared using real-time PCR procedures. Real-time PCR was performed with the Taqman<sup>TM</sup> procedure using both gene specific primers and probes to determine the levels of gene expression.

Epithelial cells were enriched from blood samples using an immunomagnetic bead separation method (Dynal A.S., Oslo, Norway). Isolated cells were lysed and the magnetic beads removed. The lysate was then processed for poly A+ mRNA isolation using magnetic beads coated with Oligo(dT)25. After washing the beads in buffer, bead/poly A+ RNA samples were suspended in 10 mM Tris HCl pH 8.0 and subjected to reversed transcription. The resulting cDNA was subjected to real-time PCR using gene specific primers. Beta-actin content was also determined and used for normalization. Samples with P501S copies greater than the mean of the normal samples + 3 standard deviations were considered positive. Real time PCR on blood samples was performed using the Taqman<sup>TM</sup> procedure but extending to 50 cycles using forward and reverse primers and probes specific for P501S. Of the eight samples tested, 6 were positive for P501S and β-actin signal. The remaining 2 samples had no detectable β-actin or P501S. No P501S signal was observed in the four normal blood samples tested.

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#### **EXAMPLE 22**

EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGENS P703P AND P501S IN SCID MOUSE-PASSAGED PROSTATE TUMORS

When considering the effectiveness of antigens in the treatment of prostate cancer, the continued presence of the antigens in tumors during androgen

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ablation therapy is important. The presence of the prostate-specific antigens P703P and P501S in prostate tumor samples grown in SCID mice in the presence of testosterone was evaluated as follows.

Two prostate tumors that had metastasized to the bone were removed from patients, implanted into SCID mice and grown in the presence of testosterone. Tumors were evaluated for mRNA expression of P703P, P501S and PSA using quantitative real time PCR with the SYBR green assay method. Expression of P703P and P501S in a prostate tumor was used as a positive control and the absence in normal intestine and normal heart as negative controls. In both cases, the specific mRNA was present in late passage tumors. Since the bone metastases were grown in the presence of testosterone, this implies that the presence of these genes would not be lost during androgen ablation therapy.

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15 ANTI-P503S MONOCLONAL ANTIBODY INHIBITS TUMOR GROWTH IN VIVO

The ability of the anti-P503S monoclonal antibody 20D4 to suppress tumor formation in mice was examined as follows.

Ten SCID mice were injected subcutaneously with HEK293 cells that expressed P503S. Five mice received 150 micrograms of 20D4 intravenously at day 0 (time of tumor cell injection), day 5 and day 9. Tumor size was measured for 50 days. Of the five animals that received no 20D4, three formed detectable tumors after about 2 weeks which continued to enlarge throughout the study. In contrast, none of the five mice that received 20D4 formed tumors. These results demonstrate that the anti-P503S Mab 20D4 displays potent anti-tumor activity *in vivo*.

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## EXAMPLE 24

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# CHARACTERIZATION OF A T CELL RECEPTOR CLONE FROM A P501S-SPECIFIC T CELL CLONE

T cells have a limited lifespan. However, cloning of T cell receptor (TCR) chains and subsequent transfer essentially enables infinite propagation of the T

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cell specificity. Cloning of tumor-antigen TCR chains allows the transfer of the specificity into T cells isolated from patients that share the TCR MHC-restricting allele. Such T cells could then be expanded and used in adoptive transfer settings to introduce the tumor antigen specificity into patients carrying tumors that express the antigen. T cell receptor alpha and beta chains from a CD8 T cell clone specific for the prostate-specific antigen P501S were isolated and sequenced as follows.

Total mRNA from 2 x 10<sup>6</sup> cells from CTL clone 4E5 (described above in Example 12) was isolated using Trizol reagent and cDNA was synthesized. To determine Va and Vb sequences in this clone, a panel of Va and Vb subtype-specific primers was synthesized and used in RT-PCR reactions with cDNA generated from each of the clones. The RT-PCR reactions demonstrated that each of the clones expressed a common Vb sequence that corresponded to the Vb7 subfamily. Futhermore, using cDNA generated from the clone, the Va sequence expressed was determined to be Va6. To clone the full TCR alpha and beta chains from clone 4E5, primers were designed that spanned the initiator and terminator-coding TCR nucleotides. The primers were as follows: TCR Valpha-6 5'(sense): GGATCC---GCCGCCACC—ATGTCACTTTCTAGCCTGCT (SEQ ID NO: 756) BamHI site Kozak TCR alpha sequence TCR alpha 3' (antisense): GTCGAC---TCAGCTGGACCACAGCCGCAG (SEQ ID NO: 757) Sall site TCR alpha constant sequence TCR Vbeta-7. 5'(sense): GGATCC---GCCGCCACC--ATGGGCTGCAGGCTGCTCT (SEQ ID NO: 758) BamHI site Kozak TCR alpha sequence TCR beta 3' (antisense): GTCGAC---TCAGAAATCCTTTCTCTTGAC (SEQ ID NO: 759) Sall site TCR beta constant sequence. Standard 35 cycle RT-PCR reactions were established using cDNA synthesized from the CTL clone and the above primers, employing the proofreading thermostable polymerase PWO (Roche, Nutley, NJ).

The resultant specific bands (approx. 850 bp for alpha and approx. 950 for beta) were ligated into the PCR blunt vector (Invitrogen) and transformed into *E. coli*. *E. coli* transformed with plasmids containing full-length alpha and beta chains were identified, and large scale preparations of the corresponding plasmids were generated. Plasmids containing full-length TCR alpha and beta chains were submitted

for sequencing. The sequencing reactions demonstrated the cloning of full-length TCR alpha and beta chains with the determined cDNA sequences for the Vb and Va chains being shown in SEQ ID NO: 760 and 761, respectively. The corresponding amino acid sequences are shown in SEQ ID NO: 762 and 763, respectively. The Va sequence was shown by nucleotide sequence alignment to be 99% identical (347/348) to Va6.2, and the Vb to be 99% identical to Vb7 (336/338),

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From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

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#### **CLAIMS**

#### What is Claimed:

- 1. An isolated polynucleotide comprising a sequence selected from the group consisting of:
- (a) sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 and 786-788:
- (b) complements of the sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 and 786-788;
- (c) sequences consisting of at least 20 contiguous residues of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 and 786-788;
- (d) sequences that hybridize to a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 and 786-788 under moderately stringent conditions;
- (e) sequences having at least 75% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-

375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 and 786-788;

- (f) sequences having at least 90% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 and 786-788; and
- (g) degenerate variants of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 and 786-788.
- 2. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

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- (a) sequences recited in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 627-629, 632, 633, 635, 637, 638, 656-671, 675, 683, 684, 710, 712, 714, 715, 717-719, 723-734, 736, 740-750, 752, 754, 755, 766-772, 777-785 and 789-791;
  - (b) sequences having at least 70% identity to a sequence of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 627-629, 632, 633, 635, 637, 638, 656-671, 675, 683, 684, 710, 712, 714, 715, 717-719, 723-734, 736, 740-750, 752, 754, 755, 766-772, 777-785 and 789-791;
    - (c) sequences having at least 90% identity to a sequence of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 627-

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629, 632, 633, 635, 637, 638, 656-671, 675, 683, 684, 710, 712, 714, 715, 717-719, 723-734, 736, 740-750, 752, 754, 755, 766-772, 777-785 and 789-791;

- (d) sequences encoded by a polynucleotide of claim 1;
- (e) sequences having at least 70% identity to a sequence encoded by a polynucleotide of claim 1; and
- (f) sequences having at least 90% identity to a sequence encoded by a polynucleotide of claim 1.
- 3. An expression vector comprising a polynucleotide of claim 1 operably linked to an expression control sequence.
- 4. A host cell transformed or transfected with an expression vector according to claim 3.
- 5. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a polypeptide of claim 2.
- 6. A method for detecting the presence of a cancer in a patient, comprising the steps of:
  - (a) obtaining a biological sample from the patient;
- (b) contacting the biological sample with a binding agent that binds to a polypeptide of claim 2;
- (c) detecting in the sample an amount of polypeptide that binds to the binding agent; and
- (d) comparing the amount of polypeptide to a predetermined cut-off value and therefrom determining the presence of a cancer in the patient.
- 7. A fusion protein comprising at least one polypeptide according to claim 2.

- 8. The fusion protein of claim 7, wherein the fusion protein comprises a sequence selected from the group consisting of:
- (a) sequences provided in SEQ ID NO: 682, 692, 695, 699, 703 and 709; and
- (b) sequences encoded by SEQ ID NO: 679, 691, 696, 700, 704 and 708.
- 9. An oligonucleotide that hybridizes to a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-626, 630, 631, 634, 636, 639-655, 674, 680, 681, 711, 713, 716, 720-722, 735, 737-739, 751, 753, 764, 765, 773-776 or 786-788 under moderately stringent conditions.
- 10. A method for stimulating and/or expanding T cells specific for a tumor protein, comprising contacting T cells with at least one component selected from the group consisting of:

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- (a) polypeptides according to claim 2;
- (b) polynucleotides according to claim 1; and
- (c) antigen-presenting cells that express a polypeptide according to claim 1,

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

11. An isolated T cell population, comprising T cells prepared according to the method of claim 10.

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- 12. A composition comprising a first component selected from the group consisting of physiologically acceptable carriers and immunostimulants, and a second component selected from the group consisting of:
  - (a) polypeptides according to claim 2;
  - (b) polynucleotides according to claim 1;
  - (c) antibodies according to claim 5;
  - (d) fusion proteins according to claim 7;
  - (e) T cell populations according to claim 11; and
- (f) antigen presenting cells that express a polypeptide according to claim 2.
- 13. A method for stimulating an immune response in a patient, comprising administering to the patient a composition of claim 12.
- 14. A method for the treatment of a cancer in a patient, comprising administering to the patient a composition of claim 12.
- 15. A method for determining the presence of a cancer in a patient, comprising the steps of:
  - (a) obtaining a biological sample from the patient;
- (b) contacting the biological sample with an oligonucleotide according to claim 9;
- (c) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and
- (d) compare the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence of the cancer in the patient.
- 16. A diagnostic kit comprising at least one oligonucleotide according to claim 9.

- 17. A diagnostic kit comprising at least one antibody according to claim 5 and a detection reagent, wherein the detection reagent comprises a reporter group.
- 18. A method for inhibiting the development of a cancer in a patient, comprising the steps of:
- (a) incubating CD4+ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of: (i) polypeptides according to claim 2; (ii) polynucleotides according to claim 1; and (iii) antigen presenting cells that express a polypeptide of claim 2, such that T cell proliferate; and
- (b) administering to the patient an effective amount of the proliferated T cells,

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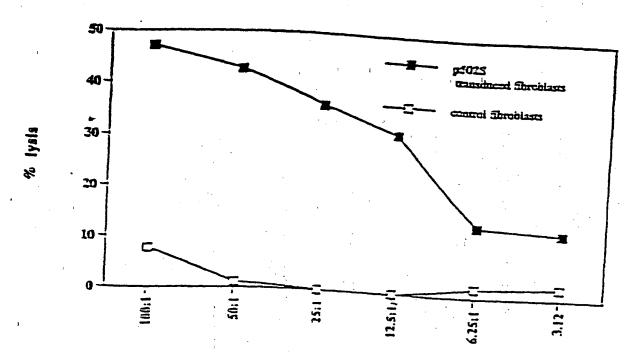
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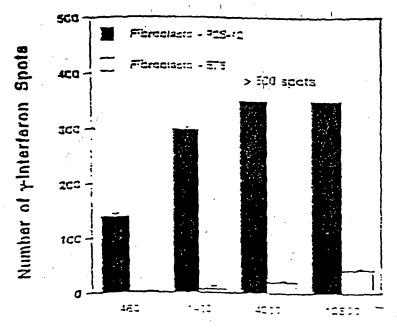
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Effector: Target Ratio

Fig. 1



Number of Responders

Fig. 2A

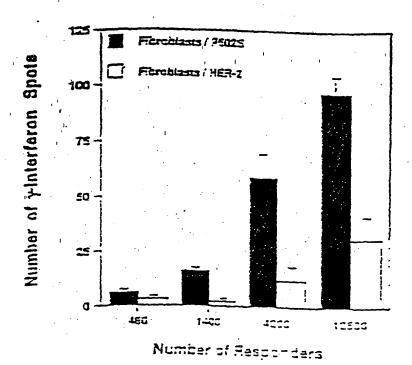


Fig. 25

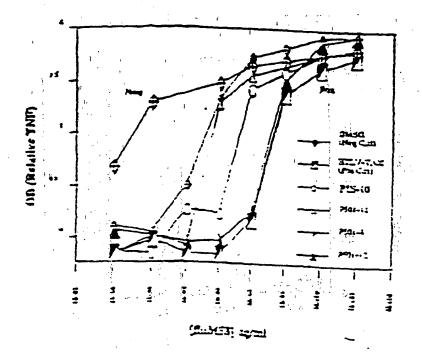


Fig. 3

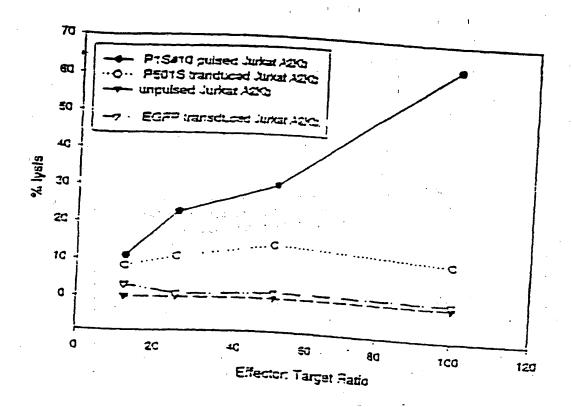


Fig. 4

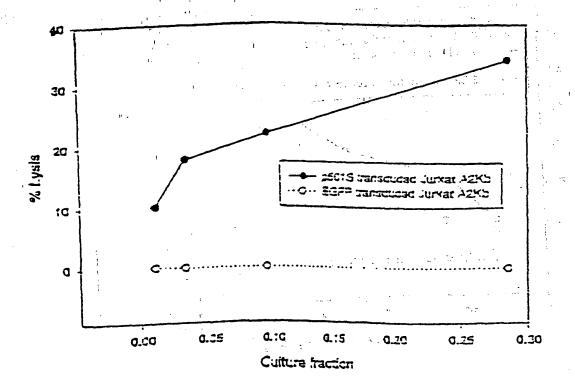
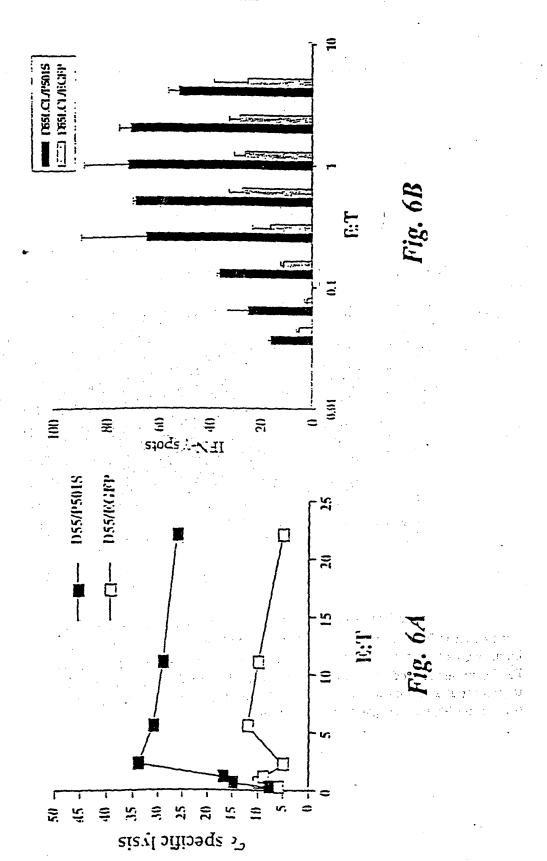
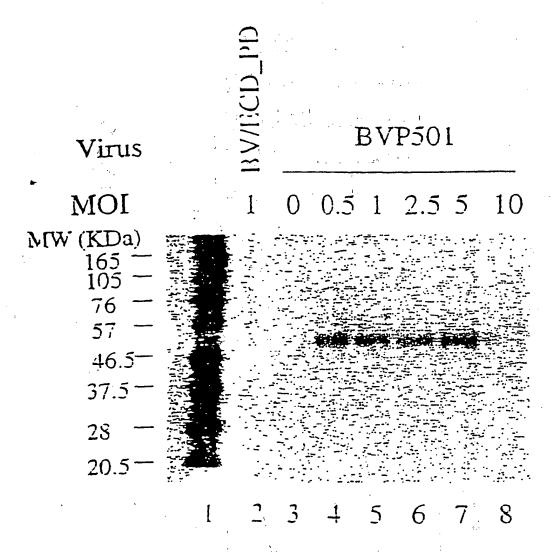


Fig. 5



Expression of P501S by the Baculovirus Expression System



0.6 million high 5 to 15 or 5-well place were infected with an unrelated control virus BV/ECD\_PD (law) 1. without virus (lane 3), or with recombinant baculovirus for P501 at different 10 lbs (lane 4 - 8). Cell lysates were run on SDS-PAGE under the reducing community and analyzed by Western blot with a monoclonal antibody against Form 15 P501S-10E3-G4D3). Lanc 1 is the biotinylated protein molecular weight market. Sublabs.

Fig. 7



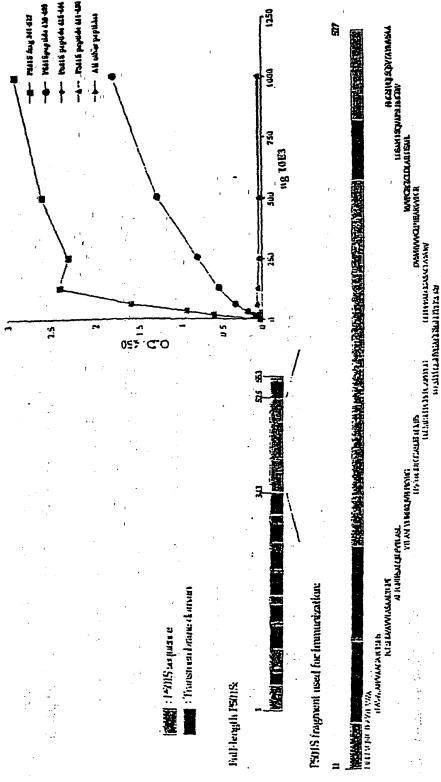


Fig. 8

## transmembrane, cytoplasmic, and extracellular regions Figure 1. Schematic of P501S with predicted

AIVQRIMVSHIJRIRK AQIJILVNILITIFQI,EVÇT, AAÇITT VVPPLIJI.EVGVREKFM TNIVLOIOPYLOI.YCYPLLGSAS

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FALLSDERDPICRO AYSYYAPABISLOGITOYITPAL DWITISALAPYLATIQICE

CLIGHTICHETICYNATHLY AREAALOPTEPAEGESAPSISPIRCPCRARIAFRNIGALLPRI.

HOLCT RAITERE LEPYARI CSWMAI MITETE FYTDIF VGLEGLYOGVFILAROTEARRIYDEGVIL

MOSLGLITOCAISLYFSLYM DRIYQRFGTRAYTLS YAAIPYAAGATGLSHSYAYYTA SAA

LTGETFSALOULPYTLASLY HREKQVFLPKYRGDTGGASSEDSIAITSFLPGPKPGAPFPNGHVGAGGSGL

LPPPPALCGASACDVSVRIVVGEPTEARVVPGRG ICLINGARILISQVAPSLE MGSIVQLSQS

## YTAYMYSAAGLGLVALYFAT QVVFDKSDLAKYSA

India sequence: Predicted intracellular domain. Sequence in hold/undudined: used to generate polyclonal rabbit serum Uniterlined sequence: Predicted transmembrane domain; Bold sequence: Predicted extracellular domain;

Governing Amino Acid Composition of Integral Membrane Proteins: Applications to topology Prediction. J.Mol Biol. 283, Localization of domains predicted using HMMTOP (G.R. Tusnady and I. Simon (1998) Principles



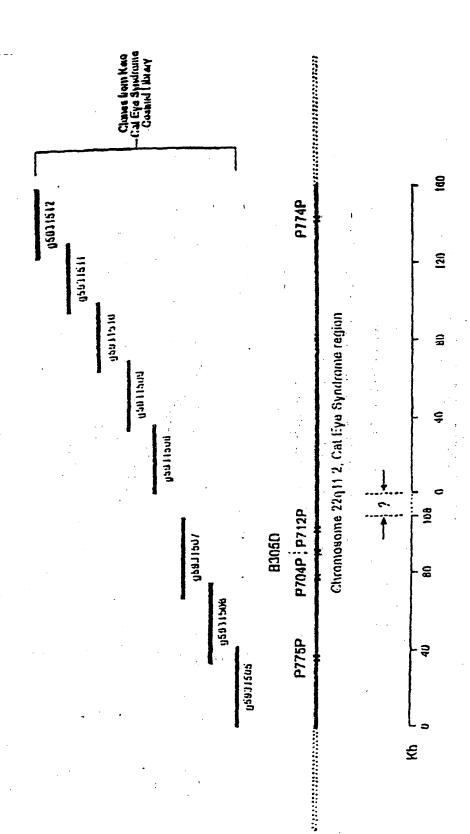


Fig. 10

## FIGURE 4. Elisa assay of rabbit polyclonal

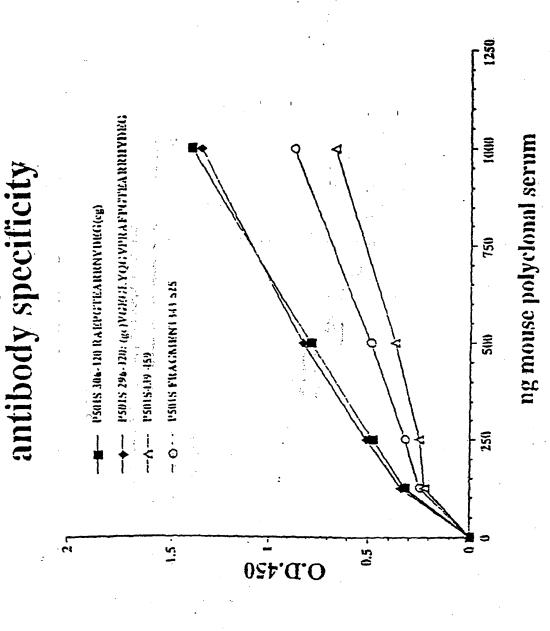


Fig. 11

## SEQUENCE LISTING

<110> Corixa Corporation Smithkline Beechan Biologicals S.A. Xu, Jiangchun Dillon, Davin C. Mitcham, Jennifer L. Harlocker, Susan L. Jiang, Yuqui Reed, Steven G. Kalos, Michael D. Fanger, Gary R. Retter, Marc W. Stolk, John A. Day, Craig H. Skeiky, Yasir A.W. Wang, Aijun Meagher, Medeleine Joy Vanderbrugge, Didier Dewerchin, Marianne Dehottay, Ph. de Rop, Philippe

<120> COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER

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720
 tetteegett etegeteact nanteetgeg eteggtentt eggetgeggg gaaeggtate
                                                                              780
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        \langle 223 \rangle n = A, T, C or G
                                                        **; .
        <400> 2
  acagaaatqt tqqatqqtqq aqcacctttc tatacgactt acaggacagc agatqqggaa
                                                                               60
  ttcatqqctq ttqqaqcaat agaaccccag ttctacgagc tgctgatcaa aggacttgga
                                                                              120
  ctaaagtctg atgaacttcc caatcagatg agcatggatg attggccaga aatgaagaag
                                                                              180
                                                                              240
  aagtttgcag atgtatttgc aaagaagacg aaggcagagt ggtgtcaaat ctttgacggc
  acagatgect gtgtgactec ggttetgact tttgaggagg ttgttcatca tgatcacaac
                                                                              300
  aaggaacggg getegtttat caccagtgag gagcaggacg tgagcccccg ccctgcacct
                                                                              360
  ctgctgttaa acaccccagc catcccttct ttcaaaaggg atccactagt tctagaagcg
                                                                              420
  geogecaccy eggtggaget ceagettttg tteeetttag tgagggttaa ttgegegett
                                                                              480
  ggcgtaatca tggtcatagc tgtttcctgt gtgaaattgt tatccgctca caattccccc
                                                                              540
  aacatacqaq ccggaacata aagtgttaag cctggggtgc ctaatgantg agctaacten
                                                                              600
  cattaattgc gttgcgctca ctgcccgctt tccagtcggg aaaactgtcg tgccactgcn
                                                                              660
  ttantgaatc ngccacccc cgggaaaagg cggttgcntt ttgggcctct tccgctttcc
                                                                              720
  tegetcattg atcetngene ceggtetteg getgeggnga aeggtteact ecteaaagge
                                                                              780
  ggtntnccgg ttatccccaa acnggggata cccnga
                                                                              816
        <210> 3
        <211> 773
        <212> DNA
        <213> Homo sapien
        <220>
        <221> misc feature
        <222> (1) ... (773)
        <223> n = A, T, C or G
        <400> 3
  cttttgaaag aagggatggc tggggtgttt aacagcagag gtgcagggcg ggggctcacg
  tectgetect cactggtgat aaacgageee egtteettgt tgtgateatg atgaacaace
                                                                              120
  tecteaaaag teagaacegg agteacaeag geatetgtge egteaaagat ttgacaecae
  totgoottog tottotttgo aaatacatot goaaacttot tottoattto tggocaatca
                                                                             240
  tccatgctca tctgattggg aagttcatca gactttagtc canntccttt gatcagcagc
                                                                              300
 tegtagaact ggggttetat tgeteeaaca geeatgaatt eeceatetge tgteetgtaa
                                                                              360
 gtcgtataga aaggtgctcc accatecaac atgttctgtc ctcgaggggg ggcccggtac 🗼 😘 420
ccaattcgcc ctatantgag tcgtattacg cgcgctcact ggccgtcgtt ttacaacgtc 480
  gtgactggga aaaccctggg cgttaccaac ttaatcgcct tgcagcacat ccccctttcg
  ccagctgggc gtaatancga aaaggcccgc accgatcgcc cttccaacag ttgcgcacct
  gaatgggnaa atgggacccc cctgttaecg cgcattnaac ccccgcnggg tttngttgtt 660
  acceccaent nnacegetta caetttgeca gegeettane gecegetece tttencettt : 1720
  ettecettee ttteneneen ettteceeeg gggttteeee enteaaacee enamen / //// 773
                  ေသည်။ ကိုမည်းနှင့် အာဏ္ဏာရာခံသည်။ သိန်း ၅၀ ကြန်လာ ကိုမည်သို့ လေသည် အမြောင်းရှိသည်။ အလုပ်မြောင်းသည်။ သိန်း
ကို သည် သင့် သည် သည် သူ့လေးသည်သည် သည် အသည် သည် သည် ရေးနှာနှင့် အမေါကာကြေသည်။
ကို သည် သည် သည် သည်သည် သည်သည် အသည်သည် သည် သည့်သည် သည်များသည် အသည်သည်။
        <211> 828
        <212> DNA
                               nite minni Siling - Saena Sili nageñagezan el est ur
```

```
<213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (828)
      <223> n = A, T, C or G
      <400> 4
cctcctgagt cctactgacc tgtgctttct ggtgtggagt ccagggctgc taggaaaagg
                                                                      60
aatgggcaga cacaggtgta tgccaatgtt tctgaaatgg gtataatttc gtcctctcct
                                                                      120
teggaacact ggetgtetet gaagacttet egeteagttt cagtgaggae acacacaaag
                                                                     180
acgtgggtga ccatgttgtt tgtggggtgc agagatggga ggggtggggc ccaccctgga
                                                                      240
agagtggaca gtgacacaag gtggacactc tctacagatc actgaggata agctggagcc
                                                                     300
acaatgcatg aggcacacac acagcaagga tgacnotgta aacatagccc acgctgtcct
                                                                      360
gngggcactg ggaagcctan atnaggccgt gagcanaaag aaggggagga tccactagtt
                                                                      420
ctanagogge cgccaccgcg gtgganctcc ancttttgtt ccctttagtg agggttaatt
                                                                      480
gegegettgg entaateatg gteataneth ttteetgtgt gaaattgtta teegeteaea
                                                                     540
attecacaca acatacgane eggaaacata aantgtaaac etggggtgee taatgantga
                                                                      600
ctaactcaca ttaattgcgt tgcgctcact gcccgctttc caatcnggaa acctgtcttg
                                                                      660
concttgcat tnatgaaton gccaaccccc ggggaaaagc gtttgcgttt tgggcgctct
                                                                     720
teegetteet eneteantta nteectnene teggteatte eggetgenge aaaceggtte
                                                                     780
accnecteea aagggggtat teeggtttee cenaateegg gganance
                                                                     828
      <210> 5
      <211> 834
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (834)
      <223> n = A, T, C or G
      <400> 5
ttttttttt tttttactga tagatggaat ttattaaget tttcacatgt gatagcacat
                                                                      60
agttttaatt gcatccaaag tactaacaaa aactctagca atcaagaatg gcagcatgtt
                                                                     120
attttataac aatcaacacc tgtggctttt aaaatttggt tttcataaga taatttatac
                                                                     180
tgaagtaaat ctagccatgc ttttaaaaaa tgctttaggt cactccaagc ttggcagtta
                                                                     240
acatttggca taaacaataa taaaacaatc acaatttaat aaataacaaa tacaacattg
                                                                     300
taggccataa tcatatacag tataaggaaa aggtggtagt gttgagtaag cagttattag
                                                                     360
aatagaatac cttggcctct atgcaaatat gtctagacac tttgattcac tcagccctga
                                                                     420
cattcagttt tcaaagtagg agacaggttc tacagtatca ttttacagtt tccaacacat
                                                                     480
tgaaaacaag tagaaaatga tgagttgatt tttattaatg cattacatcc tcaagagtta
                                                                     540
tcaccaaccc ctcagttata aaaaattttc aagttatatt agtcatataa cttggtgtgc
                                                                     600
ttattttaaa ttagtgctaa atggattaag tgaagacaac aatggtcccc taatgtgatt
                                                                     660
gatattggtc attittacca gcttctaaat ctnaactttc aggcttttga actggaacat
                                                                     720
tgnatnacag tgttccanag ttncaaccta ctggaacatt acagtgtgct tgattcaaaa
                                                                     780
tgttattttg ttaaaaatta aattttaacc tggtggaaaa ataatttgaa atna
                                                                     834
      <210> 6
                                                  <211> 818
      <212> DNA
      <213> Homo sapien
     <220>
<221> misc_feature
<222>:(1)...(818)
     <223> n = A, T, C \text{ or } G
```

```
<400> 6
                                                                        60
tttttttt ttttttt aagaccctca tcaatagatg gagacataca gaaatagtca
aaccacatct acaaaatgcc agtatcaggc ggcggcttcg aagccaaagt gatgtttgga
                                                                       120
                                                                       180
tgtaaagtga aatattagtt ggcggatgaa gcagatagtg aggaaagttg agccaataat
gacgtgaagt ccgtggaagc ctgtggctac aaaaaatgtt gagccgtaga tgccgtcgga
                                                                       240
aatggtgaag ggagactcga agtactctga ggcttgtagg agggtaaaat agagacccag
                                                                       300
                                                                       360
taaaattgta ataagcagtg cttgaattat ttggtttcgg ttgtttcta ttagactatg
gtgagctcag gtgattgata ctcctgatgc gagtaatacg gatgtgttta ggagtgggac
                                                                       420
ttctagggga tttagcgggg tgatgcctgt tgggggccag tgccctccta gttggggggt
                                                                       480
aggggctagg ctggagtggt aaaaggctca gaaaaatcct gcgaagaaaa aaacttctga
                                                                       540
ggtaataaat aggattatcc cgtatcgaag gcctttttgg acaggtggtg tgtggtggcc
ttggtatgtg ctttctcgtg ttacatcgcg ccatcattgg tatatggtta gtgtgttggg
                                                                       660
                                                                       720
ttantanggo ctantatgaa gaacttttgg antggaatta aatcaatngo ttggccggaa
gtcattanga nggctnaaaa ggccctgtta ngggtctggg ctnggtttta cccnacccat 780
greattanga nggetnaaaa ggeeetgita ngggtetggg etnggtetta eeenaeeat 760 ggaatnenee eeeeggaena ntgnateeet attettaa 818

<210> 7

<211> 817

<212> DNA

<213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (817)
      <223> n = A, T, C or G
      <400> 7
 ttttttttt tttttttt tggctctaga gggggtagag ggggtgctat agggtaaata
                                                                        60
                                                                       120
 cgggccctat ttcaaagatt tttaggggaa ttaattctag gacgatgggt atgaaactgt
 ggtttgctcc acagatttca gagcattgac cgtagtatac ccccggtcgt gtagcggtga
                                                                       180
                                                                       240
 aagtggtttg gtttagacgt ccgggaattg catctgtttt taagcctaat gtggggacag
 ctcatgagtg caagacgtct tgtgatgtaa ttattatacn aatgggggct tcaatcggga
                                                                       300
 gtactactcg attgtcaacg tcaaggagtc gcaggtcgcc tggttctagg aataatgggg
                                                                       360
 gaagtatgta ggaattgaag attaatccgc cgtagtcggt gttctcctag gttcaatacc
                                                                       420
 attggtggcc aattgatttg atggtaaggg gagggatcgt tgaactcgtc tgttatgtaa
                                                                       480
aggatnoctt ngggatggga aggcnatnaa ggactangga tnaatggcgg gcangatatt 540
 tcaaacngtc tctanttcct gaaacgtctg aaatgttaat aanaattaan tttngttatt
                                                                       600
gaatnttnng gaaaagggct tacaggacta gaaaccaaat angaaaanta atnntaangg 660
 cnttatentn aaaggtnata accnetecta tnateceace caatngnatt ecceaenenn
acnattggat neceeantte canaaangge eneceeegg tgnanneene ettttgttee
 cttnantgan ggttattcnc ccctngcntt atcancc
<210> 8
<211> 799
<212> DNA
<213> Homo sapien
       <220>
       <221> misc feature
                                                             :13 -. .
       <222> (1)...(799)
       <223> n = A, T, C or G
                                                             122
                                                     Of the State of the State of
       <400> 8
 cattteeggg tttactttet aaggaaagee gageggaage tgetaaegtg ggaateggtg
                                                                        120
 cataaggaga actttctgct ggcacgcgct agggacaagc gggagagcga ctccgagcgt
                                                                       180
 ctgaagcgca cgtcccagaa ggtggacttg gcactgaaac agctgggaca catccgcgag
 tacgaacage geetgaaagt getggagegg gaggtecage agtgtageeg egteetgggg
                                                                       240
```

```
tgggtggccg angectgane egetetgeet tgctgcccc angtgggccg ecaccccctg
                                                                       300
 acctgcctgy gtccaaacac tgagccctgc tggcggactt caagganaac ccccacangg
                                                                        360
 ggattttgct cctanantaa ggctcatctg ggcctcggcc ccccacctg gttggccttg
                                                                       420
 tetttgangt gagececatg tecatetggg ceaetgteng gaceaeettt ngggagtgtt
                                                                       480
 ctccttacaa ccacannatg cccggctcct cccggaaacc anteccance tgngaaggat
                                                                       540
 caagneetgn atccactnnt netanaaceg geenceneeg engtggaace encettntgt
                                                                       600
 tecttttent tnagggttaa tnnegcettg geettneean ngteetnene ntttteennt
                                                                       660
 gttnaaattg ttangeneee neennteeen ennennenan eeegaeeenn annttnnann
                                                                       720
 nectgggggt necnnengat tgaccennec necetntant tgenttnggg nnenntgeec
                                                                       780
ctttccctct nggganncg
                                                                       799
       <210> 9
       <211> 801
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc feature
       <222> (1)...(801)
       <223> n = A, T, C or G
      <400> 9
acgccttgat cctcccaggc tgggactggt tctgggagga gccgggcatg ctgtggtttg
                                                                        60
taangatgac actoccaaag gtggtcctga cagtggccca gatggacatg gggctcacct
                                                                       120
caaggacaag gccaccaggt gcgggggccg aagcccacat gatccttact ctatgagcaa
                                                                       180
aatcccctgt gggggcttct ccttgaagtc cgccancagg gctcagtctt tggacccang
                                                                       240
caggicatgg ggitgingne caactggggg ceneaacgea aaanggenea gggeetengn
                                                                       300
cacccatece angaegegge tacactnetg gaeeteeene tecaccaett teatgegetg
                                                                       360
ttcntacccg cgnatntgtc ccanctgttt cngtgccnac tccancttct nggacgtgcg
                                                                       420
ctacatacgc ccggantonc notcccgctt tgtccctatc cacgtnccan caacaaattt
                                                                       480
encentantg cacenattee caentttnne agnttteene nnegngette ettntaaaag
                                                                       540
ggttganccc cggaaaatnc cccaaagggg gggggccngg tacccaactn ccccctnata
                                                                       600
getgaantee eeatnaeenn gnetenatgg ancenteent tttaannaen ttetnaactt
                                                                       660
gggaanance etegneentn ecceenttaa teceneettg enangment ecceenntee
                                                                       720
necennntng gentntnann enaaaaagge eennnaneaa teteetnnen eeteantteg
                                                                       780
ccancecteg aaateggeen e
      <210> 10
      <211> 789
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(789)
      <223> n = A, T, C or G
      <400> 10
cagtetaint ggccagtgtg gcagetttee etgtggetge eggtgeeaca tgeetgteee
acagtgtggc cgtggtgaca gcttcagccg ccctcaccgg gttcaccttc tcagccctgc
                                                                      120
agatectgee etacaeactg geeteectet accaeeggga gaageaggtg tteetgeeca
                                                                      180
aataccgagg ggacactgga ggtgctagca gtgaggacag cctgatgacc agcttcctgc
                                                                      240
caggeeetaa geetggaget eeetteeeta atggacaegt gggtgetgga ggeagtggee
                                                                      300
tgctcccacc tccacccgcg ctctgcgggg cctctgcctg tgatgtctcc gtacgtgtgg
                                                                      360
tggtgggtga gcccaccgan gccagggtgg ttccgggccg gggcatctgc ctggacctcg
                                                                      420
ccatcctgga tagtgettcc tgctgtccca ngtggcccca tccctgttta tgggctccat
                                                                      480
tgtccagete agecagtetg teactgeeta tatggtgtet geegeaggee tgggtetggt
                                                                      540
cccatttact ttgctacaca ggtantattt gacaagaacg anttggccaa atactcagcg
                                                                      600
```

| ttaaaaaatt ccagcaacat tgggggtgga<br>tcctgttaac cccatggggc tgccggcttg<br>gtggctctct gctgccacct gttgctggct<br>ggngttccc                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | gccgccaatt t                                                                                                                                                                 | ctgttgctg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | ccaaantnat                                                                                                                                                           | 660<br>720<br>780<br>789                                                               |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| <210> 11<br><211> 772<br><212> DNA<br><213> Homo sapien                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                              | A TERRETOR OF THE STATE OF THE |                                                                                                                                                                      |                                                                                        |
| <220> <221> misc_feature <222> (1)(772) <223> n = A,T,C or G                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                              | , 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                      | `.<br>`                                                                                |
| <400> 11 cccaccctac ccaaatatta gacaccaaca tttgttaaat aaataagtta aatatttaaa accaacagge cacatcctga taaaaggtaa tgtgggctga ggggacctgg ttcttgtgtg actttcatat gttcaaatce catggaggag ctacattaaa cgaagetgca ggttaagggg tattcagete ccaaaaacce ttctctaggt ctgagcctgg gtaatccacc tgcagagtee ctccctgtat aqtccagac tgaaacccc aactggggaa aaaagaaaag gacgccccan gcacagggtg gcagcaaaaa aaccacttta accccggcac cccnangggg gttaacagga                                                                                                                                                                            | tgcctgtgtc tgaggggggtg gtgttcatcc tctanagatg gtgtctcaac tccgcattcca gttggaaggnc tccccagctg tcttggaaggnaa ancngggnaa c                                                        | cetgtgatgg<br>gateageaaa<br>ggactettee<br>agaaactee<br>ggaaaceagg<br>aggaggeta<br>gtgcatggaa<br>cecagteagg<br>gcanctaeg<br>acaaaaact                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | caacagaagg<br>aagacagtgc<br>cctacaaata<br>catgcaagag<br>tgactgagtt<br>gctgttaacc<br>cccttctggc<br>cagccctana<br>cacctcaaca<br>ngggggggca<br>aattnaggca               | 60<br>120<br>180<br>240<br>300<br>360<br>420<br>480<br>540<br>600<br>720               |
| ggcccnccac cccnaatntt gctgggaaat                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                              | itaaartiitt;                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | EC, Property                                                                                                                                                         |                                                                                        |
| <210> 12<br><211> 751<br><212> DNA<br><213> Homo sapien<br><220><br><221> misc_feature                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                      |                                                                                        |
| <210> 12 <211> 751 <212> DNA <213> Homo sapien  <220> <221> misc feature <222> (1)(751) <223> n = A,T,C or G  <400> 12  gccccaattc cagctgccac accaccacg agctgattga agcaacctc tacttttgg ttggctgtg tggtgacgtt gtcattgcaa aagtangtg agtcctcaaa atccgtatag atggtggtgt tccacacttg ggaagtgct ggcactacca gcaacgtcag ggaagtgct ggcactacca gcaacgtcag ggaagtgctc agcagctgcn acctcagcaa tgaagatgan caccttgct tcagtcttan caccatanca cnccggctgc gatgaagaaa tnaccccncg agtggcccna aaaatcttca aaaaggatgc ccaacagggg ctgccccacn cncnnaacga tnatnaacnt gaaccctgcn tngtggctcc aangaactcn gaagncccca cngganannc | gtgactgcat t<br>tcgtgagcct t<br>cagaatgggg g<br>ttggtgaagc c<br>agccattgtg g<br>gaggangatg a<br>gcccntgaaa a<br>ttgacaaact t<br>cccatcnatt g<br>tganccnatt g<br>tgttcaggnc c | agtteggat<br>ttgettggt<br>gaaggeact<br>cacageactt<br>cataatett<br>tgtacacea<br>agaagaacg<br>ccaananca<br>geatggeac<br>gacceceaa<br>macaagate<br>mnggeetga                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | gtcatacaaa<br>gcaggtttca<br>gttctctttg<br>gagccctttc<br>cttgatggca<br>aggcgaccac<br>tcncgagggc<br>aagaccacna<br>tggganccac<br>atgcccactg<br>tncntggtct<br>cttctnaann | 60<br>120<br>180<br>240<br>300<br>360<br>420<br>480<br>540<br>600<br>660<br>720<br>751 |

```
<213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(729)
      \langle 223 \rangle n = A,T,C or G
      <400> 13
gagecaggeg teectetgee tgeccaetea gtggeaacae eegggagetg ttttgteett
                                                                      60
tgtgganect cagcagtnec ctettteaga acteantgee aaganeeetg aacaggagee
                                                                     120
accatgoagt getteagett cattaagace atgatgatee tetteaattt geteatettt
                                                                     180
ctgtgtggtg cagccctgtt ggcagtgggc atctgggtgt caatcgatgg ggcatccttt
                                                                     240
ctgaagatet tegggeeact gtegteeagt geeatgeagt ttgteaacgt gggetactte
                                                                     300
ctcatcgcag ccggcgttgt ggtcttagct ctaggtttcc tgggctgcta tggtgctaag
                                                                     360
actgagagca agtgtgccct cgtgacgttc ttcttcatcc tcctcctcat cttcattgct
                                                                     420
gaggttgcaa tgctgtggtc gccttggtgt acaccacaat ggctgagcac ttcctgacgt
                                                                     480
tgctggtaat gcctgccatc aanaaaagat tatgggttcc caggaanact tcactcaagt
                                                                     540
qttqqaacac caccatgaaa gggctcaagt gctgtggctt cnnccaacta tacggatttt
                                                                     600
qaaganteac ctacttcaaa gaaaanagtg cctttccccc atttctgttg caattgacaa
                                                                     660
acqtccccaa cacagccaat tgaaaacctg cacccaaccc aaangggtcc ccaaccanaa
                                                                     720
                                                                     729
attnaaggg
      <210> 14
      <211> 816
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(816)
      <223> n = A, T, C or G
      <400> 14 --
tgctcttcct caaagttgtt cttgttgcca taacaaccac cataggtaaa gcgggcgcag
tgttegetga aggggttgta gtaceagege gggatgetet cettgeagag teetgtgtet
                                                                     120
ggcaggtcca cgcagtgccc tttgtcactg gggaaatgga tgcgctggag ctcgtcaaag
                                                                     180
ccactcgtgt atttttcaca ggcagcctcg tccgacgcgt cggggcagtt gggggtgtct
                                                                     240
tcacactcca ggaaactgtc natgcagcag ccattgctgc agcggaactg ggtgggctga
                                                                     300
cangtgccag agcacactgg atggcgcctt tccatgnnan gggccctgng ggaaagtccc
                                                                     360
tganceccan anetgeetet caaangeece acettgeaca eeeegacagg etagaatgga
                                                                     420
atcttcttcc cgaaaggtag ttnttcttgt tgcccaancc anccccntaa acaaactctt.
                                                                     480
quanatetqe teegnggggg tentantace ancgtgggaa aagaacecca ggengegaac
                                                                     540
caancttqtt tggatncgaa gcnataatct nctnttctgc ttggtggaca gcaccantna
                                                                     600
ctgtnnanct ttagncentg gtcctentgg gttgnncttg aacctaaten cennteaact
                                                                     660
gggacaaggt aantngcent cetttnaatt ecenanentn eeceetggtt tggggttttn
                                                                     720
cnenetecta ecceagaan neegtgttee ecceaacta ggggeenaaa cennttntte
                                                                     780
cacaaccctn ccccacccac gggttcngnt ggttng
                                                                     816
                                                              : 7
      <210> 15
                                                  <211> 783
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(783)
      \langle 223 \rangle n = A_i T_i C \text{ or } G
                               in in the August Spirit
```

```
<400> 15
                                                                                                                                                                                     60
     ccaaggcctg ggcaggcata nacttgaagg tacaacccca ggaacccctg gtgctgaagg
     atgtggaaaa cacagattgg cgcctactgc ggggtgacac ggatgtcagg gtagagagga
                                                                                                                                                                                   120
     aagacccaaa ccaggtggaa ctgtggggac tcaaggaang cacctacctg ttccagctga
                                                                                                                                                                                   180
                                                                                                                                                                                   240
     cagtgactag ctcagaccac ccagaggaca cggccaacgt cacagtcact gtgctgtcca
                                                                                                                                                                                   300
     ccaagcagac agaagactac tgcctcgcat ccaacaangt gggtcgctgc cggggctctt
                                                                                                                                                                                   360
     teccaegetg gtactatigae eccaeggage agatetgeaa gagtttegtt tatggagget
     gcttgggcaa caagaacaac taccttcggg aagaagagtg cattctancc tgtcngggtg.
                                                                                                                                                                                   420
     tgcaaggtgg gcctttgana ngcanctctg gggctcangc gactttcccc cagggcccct
                                                                                                                                                                                   480
     ccatggaaag gegecateea ntgttetetg geaectgtea geecaeceag tteegetgea
                                                                                                                                                                                   540
     ncaatggctg ctgcatcnac antttcctng aattgtgaca acacccccca ntgcccccaa
                                                                                                                                                                                   600
     ccctcccaac aaagcttccc tgttnaaaaa tacnccantt ggcttttnac aaacncccgg 660
     cncctccntt ttccccnntn aacaaagggc nctngcnttt gaactgcccn aacccnggaa
   tetneenngg aaaaantnee eeceetggtt eetnnaance eeteenenaa anetneecee
     <210> 16
<211> 801 as a series and series and series are series as a series and series are series as a series are series are series as a series are series 
                   <213> Homo sapien with the control of the control o
                   <220>
                   <221> misc_feature
                                                                                                                                                        海点 医红色反应
                    <222> (1) ... (801)
                    <223> n = A,T,C or G
                    <400> 16
     gccccaattc cagctgccac accacccacg gtgactgcat tagttcggat gtcatacaaa
     agctgattga agcaaccctc tactttttgg tcgtgagcct tttgcttggt gcaggtttca
                                                                                                                                                                                   120
     ttggctgtgt tggtgacgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg
                                                                                                                                                                                   180
     aagtagggtg agteeteaaa ateegtatag ttggtgaage cacageactt gageeettte:
                                                                                                                                                                                   240
     atggtggtgt tccacacttg agtgaagtct tcctgggaac cataatcttt cttgatggca
                                                                                                                                                                                   300
     ggcactacca gcaacgtcag gaagtgctca gccattgtgg tgtacaccaa ggcgaccaca
                                                                                                                                                                                   360
                                                                                                                                                                                   420
     gcagctgcaa cctcagcaat gaagatgagg aggaggatga agaagaacgt cncgagggca
                                                                                                                                                                                   480
     cacttgctct_ccgtcttagc accatagcag cccangaaac_caagagcaaa gaccacaacg
                                                                                                                                                                                   540
     congotgoga atgaaagaaa ntacccacgt tgacaaactg catggccact ggacgacagt
     tggcccgaan atctteagaa aagggatgcc ccatcgattg aacacceana tgcccactgc
                                                                                                                                                                                   600
     cnacaggget geneenenen gaaagaatga geeattgaag aaggatente ntggtettaa
                                                                                                                                                                                   660
     tgaactgaaa contgcatgg tggcccctgt tcagggctct tggcagtgaa ttctganaaa
                                                                                                                                                                                   720
     aaggaacngc ntnagccccc ccaaangana aaacacccc gggtgttgcc ctgaattggc
                                                                                                                                                                                   780
ggccaaggan ccctgcccn g

<210>17

<211>740

<212> DNA

<213> Homo sapien
                                                                                                                                                                                   801
                   <220>
                   <221> misc_feature
                    <222> (1)...(740)
                   <223> n = A, T, C \text{ or } G
                   <400> 17
                                                                                                                                                                                     60
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    cetttgtgga geeteageag tteeetettt cagaacteae tgecaagage cetgaacagg
                                                                                                                                                                                   120
                                                                                                                                                                                   180
    agecaccatg cagtgettea getteattaa gaccatgatg atcetettea atttgeteat
    ctttctgtgt ggtgcagccc tgttggcagt gggcatctgg gtgtcaatcg atggggcatc
                                                                                                                                                                                   240
                                                                                                                                                                                   300
    ctttctgaag atcttcgggc cactgtcgtc cagtgccatg cagtttgtca acgtgggcta
```

```
cttcctcatc gcagccggcg ttgtggtctt tgctcttggt ttcctgggct gctatggtgc
                                                                      360
taagacggag agcaagtgtg ccctcgtgac gttcttcttc atcctcctcc tcatcttcat
                                                                      420
tgctgaagtt gcagctgctg tggtcgcctt ggtgtacacc acaatggctg aaccattcct
                                                                      480
gacgttgctg gtantgcctg ccatcaanaa agattatggg ttcccaggaa aaattcactc
                                                                      540
aantntggaa caccnccatg aaaagggete caatttetgn tggetteece aactataceg
                                                                      600
gaattttgaa agantenece taetteeaaa aaaaaanant tgeetttnee eeenttetgt
                                                                      660
tgcaatgaaa acntcccaan acngccaatn aaaacctgcc cnnncaaaaa ggntcncaaa
                                                                      720
                                                                      740
caaaaaant nnaagggttn
      <210> 18
      <211> 802
      <212> DNA
      <213> Homo sapien
      ₹220>
      <221> misc_feature
      <222> (1) ... (802)
      <223> n = A, T, C or G
      <400> 18
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                                                                       60
caaggtette cagetgeege acattaegea gggcaagage etceageaac actgcatatg
                                                                     120
ggatacactt tactttagca gccagggtga caactgagag gtgtcgaagc ttattcttct
                                                                     180
gagectetgt tagtggagga agatteeggg etteagetaa gtagteageg tatgteecat
                                                                      240
aagcaaacac tgtgagcagc cggaaggtag aggcaaagtc actctcagcc agctctctaa
cattgggcat gtccagcagt tctccaaaca cgtagacacc agnggcctcc agcacctgat
                                                                      360
qqatqaqtqt qqccaqcqct gcccccttgg ccgacttggc taggagcaga aattgctcct
                                                                      420
ggttctgccc tgtcaccttc acttccgcac tcatcactgc actgagtgtg ggggacttgg
                                                                      480
getcaggatg tecagagacg tggtteegee ecetenetta atgacacegn ecanneaace
                                                                      540
gteggetece geegantgng ttegtegtne etgggteagg gtetgetgge enetaettge
                                                                      600
aancttegte nggeceatgg aatteacene aceggaactn gtangateea etnnttetat
                                                                      660
aaccggncgc caccgcnnnt ggaactccac tettnttncc tttacttgag ggttaaggtc
                                                                      720
accettnncg ttacettggt ccaaacentn centgtgteg anatngtnaa tenggneena
                                                                      780
tnecaneene atangaagee ng
      <210> 19
      <211> 731
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(731)
      <223> n = A,T,C or G
      <400> 19
cnaagettee aggtnaeggg eegenaanee tgaeeenagg tancanaang eagnengegg 60
gageceaceg teaegnggng gngtetttat nggagggge ggagecacat enetggaent 120
cntgacccca actccccncc ncncantgca gtgatgagtg cagaactgaa ggtnacgtgg
                                                                     180
caggaaccaa gancaaanne tgeteennte caagteggen nagggggegg ggetggeeac
                                                                     240
geneateent enagtgetgn aaageeeenn eetgtetaet tgtttggaga aengennnga
                                                                     300
catgcccagn gttanataac nggcngagag tnantttgcc tetecettec ggctgcgcan
                                                                     360
congtntoct tagnogacat aacctgacta cttaactgaa cccnngaatc tnccncccct
                                                                     420
ccactaagct cagaacaaaa aacttcgaca ccactcantt gtcacctgnc tgctcaagta
                                                                      480
aagtgtaccc catneccaat gtntgetnga ngctetgnee tgenttangt teggteetgg
                                                                      540
quagacetat cauttnaage tatgtttetg actgeetett geteeetgna acaanenace
                                                                      600
ennennteca aggggggne ggececcaat cececcaace ntnaattnan tttanceen
                                                                      660
ecceenggee eggeettta enanentenn nnaengggna aaacennnge tttneceaac
                                                                     720
```

```
731
   nnaatcence t
              <210> 20
              <211> 754
              <212> DNA
              <213> Homo sapien
              <220>
              <221> misc_feature
              <222> (1)...(754)
              \langle 223 \rangle n = A, T, C or G
              <400> 20
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                                                                                                                                       120
   caacceccte ntecaaatnn centtteegg gngggggtte caaacccaan ttanntttgg
                                                                                                                                       180
   annttaaatt aaatnttnnt tggnggnnna anccnaatgt nangaaagtt naacccanta
   tnancttnaa tncctggaaa congtngntt ccaaaaatnt ttaaccctta antocctccg
                                                                                                                                       240
   aaatngttna nggaaaaccc aanttctcnt aaggttgttt gaaggntnaa tnaaaanccc
                                                                                                                                       300
   nnccaattgt ttttngccac gcctgaatta attggnttcc gntgttttcc nttaaaanaa
                                                                                                                                       360
   ggnnancccc ggttantnaa tccccccnnc cccaattata ccganttttt ttngaattgg
                                                                                                                                       420
   gancconcgg gaattaacgg ggnnnntecc tnttgggggg cnggnncccc ccccntcggg
   ggttngggnc aggncnnaat tgtttaaggg tccgaaaaat ccctccnaga aaaaaanctc
   ccaggntgag nntngggttt ncccccccc canggcccct ctcgnanagt tggggtttgg 600
   ggggcctggg attttntttc ccctnttncc teccccccc ccnggganag aggttngngt, 660
   tttgntcnnc ggccccnccn aaganctttn ccganttnan ttaaatccnt gcctnggcga
   agtcentegn agggntaaan ggccccetnn cggg

<210> 21

<211> 755

<212> DNA

<213> Homo sapien

<220>

<221> misc feature
              <221> misc feature
              <222> (1) ... (755) ·
              <223> n = A, T, C or G
              <400> 21
   atcaneceat gacceenaac nngggacene teaneeggne nnnenacene eggeenatea
                                                                                                                                         60
                                                                                                                                       120
   nngtnagnnc actnonnttn natcacnece encenactae gecenenane enaegeneta
                                                                                                                                       180
   nncanatnec actganngeg egangtngan ngagaaanet nataccanag neaccanaen
   ccagctgtcc nanaangcct nnnatacngg nnnatecaat ntgnancetc cnaagtattn
                                                                                                                                       240
   nnenneanat gatttteetn anecgattae centneecee taneceetee eececaaena
                                                                                                                                       300
   cgaaggenet ggneenaagg nngegnenee eegetagnte eeenneaagt eneneneeta
                                                                                                                                       360
   aactcancon nattacnego ttentgagta teacteeceg aateteacec tactcaacte
                                                                                                                                       420
   aaaaanatcn gatacaaaat aatncaagcc tgnttatnac actntgactg ggtctctatt
                                                                                                                                       480
ttagnggtcc ntnaanchtc ctaatacttc cagtctncct tcnccaattt ccnaanggct
                                                                                                                                       540
ctttcngaca gcatnttttg gttcccnntt gggttcttan ngaattgccc ttcntngaac
                                                                                                                                       600
gggctcntct tttccttcgg ttancctggn ttcnnccggc cagttattat ttcccntttt
                                                                                                                                      660
                                                                                                                                       720
   aaattentne entttanttt tggenttena aacceeegge ettgaaaaeg geeeeetggt
                                                                                                                                     755
   aaaaggttgt tttganaaaa tttttgtttt gttcc
              <213> Homo sapien, day or a transfer that the same of 
                                    ာမှာ သည်တွင်တို့မှာ ကာနေ့ မေရာသည်။ မေရာက် ကာသက် အားမနှန်မှာ သန်းမိုး မြီးရှင်မည့်မှာ စားများက
```

TOTOMORNIA ALIE TORONOCO

<221> misc\_feature

25 (22.5)

```
<222> (1)...(849)
      <223> n = A, T, C or G
tttttttttt tttttangtg tngtcgtgca ggtagaggct tactacaant gtgaanacgt
                                                                       60
acqctnggan taanqcgacc cganttctag ganncnccct aaaatcanac tgtgaagatn
                                                                      120
atcctgnnna cggaanggtc accggnngat nntgctaggg tgnccnctcc cannncnttn
                                                                      180
cataacteng nggccetgce caccacette ggeggeceng ngneegggee egggteattn
                                                                      240
gnnttaacen eactnigena neggitteen neecenneng accenggega teeggggtne
                                                                      300
tetgtettee cetgnagnen anaaantggg ceneggneee etttaceeet nnacaageea
                                                                      360
engeenteta necnengece eccetecant nngggggact geenannget ecgttnetng
                                                                      420
nnaccconn gggtncctcg gttgtcgant cnaccgnang ccanggattc cnaaggaagg
                                                                      480
tgcgttnttg gcccctaccc ttcgctncgg nncacccttc ccgacnanga nccgctcccq
                                                                      540
enconnegung cetenceteg caacaceege netentengt neggnnnece ceceaceege
                                                                      600
necetenene ngnegnanen eteeneenee gteteannea eeaeeegee eegeeaggee
                                                                      660
nteanceach ggnngaenng nagenennte geneegegen gegneneet egeenengaa
                                                                      720
ctncntcngg ccantnncgc tcaanccnna cnaaacgccg ctgcgcggcc cgnagcgncc
                                                                      780
necteenega gteeteeegn etteenacee anguntteen egaggaeaen nnaceeegee
                                                                      840
nncangcgg
      <210> 23
      <211> 872
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(872)
      <223> n = A, T, C or G
      <400> 23
gegeaaacta tacttegete gnactegtge geetegetne tetttteete egeaaceatg
                                                                       60
tetgaenane eegattngge ngatatenan aagntegane agteeaaaet gantaacaca
                                                                      120
cacacnenan aganaaatee netgeettee anagtanaen attgaaenng agaaecange
                                                                      180
nggcgaatcg taatnaggcg tgcgccgca atntgtcncc gtttattntn ccagcntcnc
                                                                      240
ctncenaccc tachtetten nagetgtenn acccetngth egnacecece naggteggga
                                                                      300
tegggtttnn nntgacegng ennecettee eccentecat nacganeene eegeaceace
                                                                      360
nanngenege neceegnnet ettegeenee etgteetnin eeeetginge etggenengn
                                                                      420
accgcattga ccctcgccnn ctncnngaaa ncgnanacgt ccgggttgnn annancgctg
                                                                      480
tgggnnngcg tctgcnccgc gttccttccn ncnncttcca ccatcttcnt tacngggtct
                                                                      540
conegeente tennneache eetgggaege thteethtge eeceetthae teeceectt
                                                                      600
egnegtgnee egneceeace nteatttnea naegntette acaannneet ggntnnetee
                                                                      660
chancing gtcancenag ggaagggngg ggnncenntg nttgacgttg nggnqangte
                                                                      720
egaanantee teneentean enetaceeet egggegnnet etengttnee aaettaneaa
                                                                      780
ntetecceeg ngngenente teageetene ceneceenet etetgeantg tnetetgete
                                                                      840
tnaccnntac gantnttcgn cnccctcttt cc
                                                                      872
      <210> 24
      <211> 815
      <212> DNA
      <213> Homo sapien
     <220>
     <221> misc feature
      <222> (1)...(815)
      <223> n = A, T, C or G
```

| <400> 24                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | •                                                                                                                                  |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------|
| gcatgcaagc ttgagtattc tatagngtca cctaaatanc tte                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | ggcntaat catggtcnta 60                                                                                                             |
| netgnettee tgtgteaaat gtataenaan tanatatgaa te                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                    |
| tentneatta gtaacaantg tnntgteeat eetgtengan car                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                    |
| cgcattcncn gencantatn taatngggaa ntennntnnn ne                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                    |
| geneectgae tggnagagat ggatnantte tnntntgace na                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                    |
| aananccccc cgcngnccac cggttngnng cnagccnntc cc                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                    |
| aacctgcgtc aganncatca aacntgggaa acccgcnncc and                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                    |
| gatecegtee aggnttnace atceettene agegeeect tt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                    |
| gtgtccnanc enctcaacat ganacgegee agnecanceg ca                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | attnggca caatgtcgnc 540                                                                                                            |
| gaacccccta gggggantna tncaaanccc caggattgtc cn                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | cncangaa atcccncanc 600                                                                                                            |
| cccnccctac ccnnctttgg gacngtgacc aantcccgga gt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | necagtee ggeengnete - 660                                                                                                          |
| cccaccggt nnccntgggg gggtgaanct cngnntcanc cn                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                    |
| accggneetn ggnegaanng anenntenga agngeenent eg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                    |
| nccnachgnt agntcccccc cngggtncgg aangg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 815                                                                                                                                |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 1                                                                                                                                  |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                    |
| <212> DNA 1 (1985) DE 2017 (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (1985) (19       | •                                                                                                                                  |
| <213> Homo sapien                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                    |
| <220>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                    |
| <221> misc_feature                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | •                                                                                                                                  |
| <222> (1)(775)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                    |
| $\langle 223 \rangle$ n = A,T,C or G                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                    |
| <400> 25                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                    |
| ccgagatgtc tcgctccgtg gccttagctg tgctcgcgct ac                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                    |
| aggetateca gegtaeteca aagatteagg tttacteacg te                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | atccagca gagaatggaa 120                                                                                                            |
| agtcaaattt cctgaattgc tatgtgtctg ggtttcatcc at                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | ccgacatt gaanttgact 180                                                                                                            |
| tactgaagaa tgganagaga attgaaaaag tggagcattc ag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                    |
| actggtettt ctatetentg tactacactg aatteaceec ca                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                    |
| cctgccgtgt gaaccatgtg actttgtcac agcccaagat ag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                    |
| tgtaagcagn cnncatggaa gtttgaagat gccgcatttg ga                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                    |
| ctgcttgctt gcnttttaat antgatatgc ntatacaccc ta                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                    |
| tgtaggggtt acatnantgt tcncntngga catgatcttc ct                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                    |
| aattgcccgt enccengttn ngaatgtttc ennaaccacg gt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                    |
| tettaeggaa gggeetggge enettineaa ggttggggga ac                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                    |
| cencencea enntettgng nnencanttt ggaaceette en                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                    |
| and the control of th       | ttccccc ttacc 775                                                                                                                  |
| nccttnncta anaaaacttn aaancgtngc naaanntttn ac                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | receded trade 775                                                                                                                  |
| 210 06                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                    |
| 00. <210> 26                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | •                                                                                                                                  |
| <211> 820                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                    |
| ZIZZ DRAY TO THE TOTAL THE TANK THE TAN       |                                                                                                                                    |
| <213> Homo sapien                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                    |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                    |
| which is a stage of the contact which is the contact of                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                    |
| <pre>clustral propagation and discretified making the continuous c</pre> |                                                                                                                                    |
| <pre>&lt;220&gt; &lt;221&gt; misc_feature</pre>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                    |
| <220> <221> misc_feature <222> (1)(820)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                    |
| <pre>&lt;220&gt; &lt;221&gt; misc_feature</pre>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                    |
| <220> <221> misc_feature <222> (1)(820)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                    |
| <220> <221> misc_feature <222> (1)(820)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                    |
| <220> <221> misc_feature <222> (1)(820) <223> n = A,T,C or G                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                    |
| <pre>&lt;220&gt;   &lt;221&gt; misc_feature   &lt;222&gt; (1)(820)   &lt;223&gt; n = A,T,C or G  &lt;400&gt; 26 anattantac agtgtaatct tttcccagag gtgtgtanag ggg</pre>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | aacggggc ctagaggcat 60                                                                                                             |
| <pre>&lt;220&gt;   &lt;221&gt; misc_feature   &lt;222&gt; (1)(820)   &lt;223&gt; n = A,T,C or G    &lt;400&gt; 26 anattantac agtgtaatct tttcccagag gtgtgtanag ggcccanagata ncttatanca acagtgcttt gaccaagagc tgccanagata</pre>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | aacggggc ctagaggcat 60<br>ctgggcac atttcctgca 120                                                                                  |
| <pre>&lt;220&gt;   &lt;221&gt; misc_feature   &lt;222&gt; (1)(820)   &lt;223&gt; n = A,T,C or G  &lt;400&gt; 26 anattantac agtgtaatct tttcccagag gtgtgtanag ggcccanagata ncttatanca acagtgcttt gaccaagagc tggaaaaggtgg cggtccccat cactcctct ctcccatagc cactcctct</pre>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | aacggggc ctagaggcat 60<br>ctgggcac atttcctgca 120<br>tcccagag gggtgagtag 180                                                       |
| <pre>&lt;220&gt;     &lt;221&gt; misc_feature     &lt;222&gt; (1)(820)     &lt;223&gt; n = A,T,C or G  &lt;400&gt; 26 anattantac agtgtaatct tttcccagag gtgtgtanag ggcccanagata ncttatanca acagtgcttt gaccaagagc tggaaaaggtgg cggtcccat cactcctct ctcccatagc caccatcangcc ttcggtggaa gggagtcang gaaacaacan accatcatcangcc ttcggtggaa gggagtcang gaaacaacan accatcatcangcc ttcggtggaa gggagtcang gaaacaacan accatcatcangcc</pre>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | aacggggc ctagaggcat 60<br>ctgggcac atttcctgca 120<br>tcccagag gggtgagtag 180<br>cacagagc anacagacca 240                            |
| <pre>&lt;220&gt;   &lt;221&gt; misc_feature   &lt;222&gt; (1)(820)   &lt;223&gt; n = A,T,C or G  &lt;400&gt; 26 anattantac agtgtaatct tttcccagag gtgtgtanag ggcccanagata ncttatanca acagtgcttt gaccaagagc tggaaaaggtgg cggtccccat cactcctct ctcccatagc cactcctct</pre>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | aacggggc ctagaggcat 60<br>ctgggcac atttcctgca 120<br>tcccagag gggtgagtag 180<br>cacagagc anacagacca 240<br>gtggcana nganagccta 300 |

| ttcctacctg acnaccagng acnnagcact cacctgeccc attncgggga gatggaattt tncccttccg tccctctntt ntcctgncnc ganattccac tnncgcctnc gggnncctcg ntcatcctct tccaaccntc gntggccntn                                                                                                                                                                        | cccatggccg<br>naccaaggga<br>gccnntcccc<br>acttttnacc<br>cntcnatcng<br>cttttcnct                                                                                      | tnegentece<br>necectect<br>tetteettta<br>cennnattte<br>naanacnaaa<br>aceneenntt                                                                        | tggtcctgnc<br>ccanctgtga<br>cacgcccct<br>ccttnattga<br>nactntctna<br>ctttgcctct                                                                        | aagggaagct<br>aggaaaaann<br>nntactcntc<br>tcggannctn<br>cccnggggat                                                                                      | 420<br>480<br>540<br>600<br>660<br>720<br>780<br>820                                          |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|
| <210> 27<br><211> 818<br><212> DNA<br><213> Homo sapio                                                                                                                                                                                                                                                                                      | an                                                                                                                                                                   | 1 1                                                                                                                                                    | 1                                                                                                                                                      |                                                                                                                                                         | ,                                                                                             |
| <220><br><221> misc_feat                                                                                                                                                                                                                                                                                                                    | ıre                                                                                                                                                                  |                                                                                                                                                        |                                                                                                                                                        |                                                                                                                                                         |                                                                                               |
| <222> (1) (810<br><223> n = A, T, C                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                      |                                                                                                                                                        |                                                                                                                                                        |                                                                                                                                                         |                                                                                               |
| <pre>&lt;400&gt; 27 tetgggtgat ggcctettec tgtttettet ccgagecca ctgcggatge tgtgacggac ctgctgagca cttcegeccc tccgcetcca gggttetget ttetteetge ccentecetg gatetcagtt tccctenete tatnacenan tggnetgtne netecettee anttennna ctcetttgee ctnaceangg ctgntnnece cnetenennt tnnetetten ngtntegnaa cnnntgnang tnnttnnnne ccennecece ngnattaagg</pre> | ggcageggtg<br>ccaaggggca<br>tcaccetgcc<br>cttccangca<br>getetgantc<br>anngaactct<br>tgtcnnactt<br>accngettnc<br>gccnnnaccg<br>tncetegtcc<br>ngntenentn<br>nengnnecce | atteageeet aatagggtee cageeetge ngceaneaag tetgtettee gtttetgann taatgggeen ententetee ceentnnetn ennennegen tnnnnngnen nnnnennnnn                     | gcccaacctg<br>cagggtccag<br>catgagctct<br>tggcgctggg<br>tgtcctgtgc<br>tcttcantta<br>gaccggctaa<br>ccntancccg<br>ggggggcnng<br>nngcannttc<br>ngntnntncn | attetgatga<br>ggagggggege<br>gggetgggte<br>ccaeactgge<br>angeneettg<br>actntgantt<br>tecetecete<br>cengggaane<br>gtnnetnene<br>nengteeenn<br>tecetetene | 60<br>120<br>180<br>240<br>300<br>360<br>420<br>480<br>540<br>600<br>660<br>720<br>780<br>818 |
| <210> 28<br><211> 731<br><212> DNA<br><213> Homo sapio                                                                                                                                                                                                                                                                                      | en                                                                                                                                                                   | N. 4                                                                                                                                                   |                                                                                                                                                        |                                                                                                                                                         |                                                                                               |
| <221> misc_featu<br><222> (1)(73<br><223> n = A,T,C                                                                                                                                                                                                                                                                                         | l)<br>or G                                                                                                                                                           |                                                                                                                                                        | 1.95                                                                                                                                                   |                                                                                                                                                         | , in the section                                                                              |
| <pre>&lt;400&gt; 28 aggaagggcg gagggatatt tcccaacatg anggtgnngt gattnaaccc cattgtatgg ntanattcct gtnaatcgga attnctcccg ggtagtgcat actaaagntt naagtgggan tnnnttncct tcgccctntg nnngcgncnc tgaaannnnc cgtttcncat naaggcactt nggttcncct acgctnntng gnaatgggta gggncttntc tctcnacccc ccccttttt</pre>                                            | gtangggatt<br>tctctttga<br>agnnaaaggn<br>aaatnatntt<br>nttngggggn<br>tncaaatgaa<br>actctgcnng<br>tcgnggctnn<br>tngcctcatc<br>cncctnnntn<br>ttttnaccnn                | gagggatagg<br>angagggttg<br>tttnagggat<br>tcnncnggaa<br>cngccangtt<br>aacctnncac<br>agcccaatac<br>gancatcang<br>caaccnctng<br>ganattttnc<br>gnggtntact | agnataangg<br>ngttttann<br>tttteggete<br>aatnttgete<br>teecaggetg<br>agagnateen<br>cenngngnat<br>gggtttegea<br>ceetenneea<br>eegeetnggg<br>aatennetne  | gggaggtgtg<br>cenggtgggt<br>ttatcagtat<br>ceatecgnaa<br>ctanaategt<br>taccegactg<br>gtenecengn<br>teaaaagenn<br>ttingcegte<br>naanceteet<br>acgentnett  |                                                                                               |

```
731
nnncccannc c
                                <210> 29
                                <211> 822
                                <212> DNA
                                <213> Homo sapien
                                <220>
                                <221> misc_feature
                                <222> (1) ... (822)
                                <223> n = A, T, C \text{ or } G
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                                                                                                                                                                                                                                                                                                                                                                                      60
 cgctcanacc tcacancctc ccnacnangc ctataangaa nannaataga nctgtncnnt
                                                                                                                                                                                                                                                                                                                                                                                 120
  atnintacne teatanneet ennnaceeae teeetettaa eeentactgi geetaingen
                                                                                                                                                                                                                                                                                                                                                                                 180
 tnnctantct ntgccgcctn cnanccaccn gtgggccnac cncnngnatt ctcnatctcc
                                                                                                                                                                                                                                                                                                                                                                                 240
  tenecatntn gectananta ngtneatace etatacetae necaatgeta nnnetaanen
                                                                                                                                                                                                                                                                                                                                                                                 300
 tecatnantt annntaacta ccactgacnt ngactttene atnaneteet aatttgaate .
                                                                                                                                                                                                                                                                                                                                                                                 360
  tactctgact cccacngcct annnattagc anchtccccc nachatntct caaccaaatc
                                                                                                                                                                                                                                                                                                                                                                                 420
  ntcaacaace tatetanetg ttenecaace nttnecteeg ateccennae aacceecete
                                                                                                                                                                                                                                                                                                                                                                                  480
ccaaatacce necacetgae nectaaccen caccateceg geaageenan ggneatttan
                                                                                                                                                                                                                                                                                                                                                                                 540
 ccaaatacce nccacetgae nectaaecen caecateceg general general general caecategaat caenatngga naaaaaaaac cenaaetete tanenennat eteeetaana aatneteetn naatttaetn neantnecat caaneecaen tgaaaennaa eecetgttt tanateeett etttegaaaa cenaeeettt annneecaae etttnggee eeceenetne
                                                                                                                                                                                                                                                                                                                                                                                  600
                                                                                                                                                                                                                                                                                                                                                                                  660
                                                                                                                                                                                                                                                                                                                                                                                 720
  conaatgaag gnoncocaat cnangaaacg noontgaaaa ancnaggona anannntocg
                                                                                                                                                                                                                                                                                                                                                                                  780
   canatoctat cocttantin ggggnccctt ncccngggcc cc
                                  <210> 30 To 85 and the second of the term of the second of
                                 <210> 30
<211> 787
<212> DNA
                                                                                                                                                                  The production of the control of What the control of the con-
                                  <213> Homo sapien

    Specifical Control of the Control of t
                                  100 miles 100 miles 100 miles 100 ft 
                                  <221> misc_feature
                                   <222> (1) ... (787)
                                   <223> n = A, T, C or G
                                   <400> 30
    cggccgcctg ctctggcaca tgcctcctga atggcatcaa aagtgatgga ctgcccattg
                                                                                                                                                                                                                                                                                                                                                                                         60
    ctagagaaga ccttctctcc tactgtcatt atggagccct gcagactgag ggctcccctt
                                                                                                                                                                                                                                                                                                                                                                                   120
    gtctgcagga tttgatgtct gaagtcgtgg agtgtggctt ggagctcctc atctacatna
                                                                                                                                                                                                                                                                                                                                                                                   180
    getggaagee etggagggee tetetegeea geeteeceet teteteeaeg etetecangg
                                                                                                                                                                                                                                                                                                                                                                                   240
                                                                                                                                                                                                                                                                                                                                                                                   300
     acaccagggg ctccaggcag cccattattc ccagnangac atggtgtttc tccacgcgga
     cccatggggc ctgnaaggcc agggtctcct ttgacaccat ctctcccgtc ctgcctggca
                                                                                                                                                                                                                                                                                                                                                                                    360
                                                                                                                                                                                                                                                                                                                                                                                    420
    ggccgtggga tccactantt ctanaacggn cgccaccncg gtgggagctc cagcttttgt
     tecenttaat gaaggttaat tgenegettg gegtaateat nggteanaae tnttteetgt
                                                                                                                                                                                                                                                                                                                                                                                     480
    gtgaaattgt ttntccctc ncnattccnc ncnacatacn aacccggaan cataaagtgt
                                                                                                                                                                                                                                                                                                                                                                                    540
    taaagcctgg gggtngcctn nngaatnaac tnaactcaat taattgcgtt ggctcatggc
                                                                                                                                                                                                                                                                                                                                                                                     600
    ccgctttccn ttcnggaaaa ctgtcntccc ctgcnttnnt gaatcggcca cccccnggg
                                                                                                                                                                                                                                                                                                                                                                                     660
    aaaagcggtt tgentittng ggggnteett eenetteece eetenetaan eeetnegeet
                                                                                                                                                                                                                                                                                                                                                                                    720
    cggtcgttnc nggtngcggg gaangggnat nnnctcccnc naagggggng agnnngntat
                                                                                                                                                                                                                                                                                                                                                                                    780
                                                     ్టులు 19 గ్రామంతి గ్రామం నుండి 19 కుంటు గ్రామం చూడితో ఉంది. కార్యాలో కార్యాలో కార్యాలో కార్యాలు
గ్రామంలో గ్రామం నుండి కార్యాలో కారులు గ్రామం కార్యాలో కార్యాలు కార్యాలు కార్యాలు కార్యాలు కార్యాలు కార్యాలు కా
                                                                                                                                                                                                                                                                                                                                                                                     787
     ccccaaa
                                    <210> 31 Table 1 respectively to the control of the
                                    <211> 799 The suppose and the suppose of the suppos
```

```
<220>
      <221> misc feature
      <222> (1)...(799)
      <223> n = A, T, C or G
      <400> 31
ttttttttt ttttttggc gatgctactg tttaattgca ggaggtgggg gtgtgtgtac
                                                                    60
catgtaccag ggctattaga agcaagaagg aaggagggag ggcagagcgc cctgctgagc
                                                                   120
aacaaaggac teetgeagee ttetetgtet gtetettgge geaggeacat ggggaggeet
                                                                   180
cccgcagggt gggggccacc agtccagggg tgggagcact acanggggtg ggagtgggtg
                                                                   240
gtggctggtn cnaatggcct gncacanatc cctacgattc ttgacacctg gatttcacca
                                                                   300
ggggacette tgttetecea nggnaactte ntnnateten aaagaacaca actgtttett
                                                                   360
engeanttet ggetgtteat ggaaageaca ggtgteenat ttnggetggg acttggtaca
                                                                   420
tatggttccg gcccacctct cccntcnaan aagtaattca ccccccccn ccntctnttg
                                                                   480
cctgggccct taantaccca caccggaact canttantta ttcatcttng gntgggcttg
                                                                   540
ntnatcnecn cetgaangeg ceaagttgaa aggecaegee gthecenete eecatagnan
                                                                   600
nttttnnent canctaatge ceeeeengge aacnateeaa teeeeeeen tgggggeeee
                                                                   660
ageceangge eccegneteg ggnnneengn enegnantee ecaggntete ecantengne
                                                                   720
conningence ecceptacea gaacanaagg ntngageene egeanninnin nggtinenae
                                                                   780
ctcgccccc ccnncgnng
                                                                   799
      <210> 32
     <211> 789
      <212> DNA
      <213> Homo sapien
                         <220>
     <221> misc feature
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     <223> n = A,T,C or G
     <400> 32
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                                                                   120
ggcaacaggc tccggcggcg gcggcggcgg ccctacctgc ggtaccaaat ntgcagcctc
                                                                   180
cgctcccgct tgatnttcct ctgcagctgc aggatgccnt aaaacagggc ctcggccntn
                                                                   240.
ggtgggcacc ctgggatttn aatttccacg ggcacaatgc ggtcgcancc cctcaccacc
                                                                   300
nattaggaat agtggtntta cccnccnccg ttggcncact ccccntggaa accacttntc
                                                                  360
gcqqctccqq catctqqtct taaaccttqc aaacnctqqq qccctctttt tqqttantnt
                                                                   420
nccnqccaca atcatnactc agactqqcnc qqqctqqccc caaaaaancn ccccaaaacc
                                                                   480
ggnccatgtc ttnncggggt tgctgcnatn tncatcacct cccgggcnca ncaggncaac
                                                                   540
ccaaaagttc ttgnggcccn caaaaaanct ccggggggnc ccaqtttcaa caaagtcatc
                                                                   600
ccccttggcc cccaaatcct cccccgntt nctgggtttg ggaacccacg cctctnnctt
                                                                   660
tggnnggcaa gntggntece cettegggee eeeggtggge cennetetaa ngaaaaenee
                                                                   720
ntectnnnea ccatecece nngnnaegne tancaangna teeettttt tanaaaeggg
                                                                   780
cccccncg
                                                or kind of the state of
     <210> 33
     <211> 793
     <212> DNA
     <213> Homo sapien
     <220>
<221> misc_feature
<222> (1)...(793)
<223> n = A,T,C or G
```

```
<400> 33
                                                                                                                                                                                                                                                  60
        qacagaacat gttggatggt ggagcacctt tctatacgac ttacaggaca gcagatgggg
                                                                                                                                                                                                                                               120
        aattcatggc tgttggagca atanaacccc agttctacga gctgctgatc aaaggacttg
                                                                                                                                                                                                                                               180
        gactaaagtc tgatgaactt cccaatcaga tgagcatgga tgattggcca gaaatgaana
                                                                                                                                                                                                                                               240
        agaagtttgc agatgtattt gcaaagaaga cgaaggcaga gtggtgtcaa atctttgacg
                                                                                                                                                                                                                                               300
        gcacagatgc ctgtgtgact ccggttctga cttttgagga ggttgttcat catgatcaca
        acaangaacg gggctcgttt atcaccantg aggagcagga cgtgagcccc cgccctgcac
                                                                                                                                                                                                                                                360
        ctctgctgtt aaacacccca gccatccctt ctttcaaaag ggatccacta cttctagagc
                                                                                                                                                                                                                                               420
      ggncgccacc gcggtggagc tccagctttt gttcccttta gtgagggtta attgcgcgct
                                                                                                                                                                                                                                               480
                                                                                                                                                                                                                                               540
        tggcgtaatc atggtcatan ctgtttcctg tgtgaaattg ttatccgctc acaattccac
        acaacatacg ancoggaage atnaaatttt aaagootggn ggtngootaa tgantgaact
                                                                                                                                                                                                                                               600
        nactcacatt aattggcttt gegeteactg eccgetttee agteeggaaa acctgteett
                                                                                                                                                                                                                                               660
        gecagetgee nttaatgaat enggeeacce eeeggggaaa aggengtttg ettnttgggg 72 720
        cgcnettece getttetege tteetgaant eetteeeee ggtetttegg ettgeggena 780
       acggtatena cet i ne investora sono ne sea de incluire a la companya de
                           <220>
                            <221> misc feature
                                                                                                                                                                                                                         4 A 🕳 🔒
                           <222> (1)...(756)
                            <223> n = A, T, C or G
                           <400> 34
        gccgcgaccg gcatgtacga gcaactcaag ggcgagtgga accgtaaaag ccccaatctt
        ancaagtgcg gggaanagct gggtcgactc aagctagttc ttctggagct caacttcttg
                                                                                                                                                                                                                                               120
        ccaaccacag ggaccaagct gaccaaacag cagctaattc tggcccgtga catactggag
                                                                                                                                                                                                                                               180
        ateggggeec aatggageat ectaegeaan gacateecet eettegageg etaeatggee
                                                                                                                                                                                                                                               240
        cagctcaaat gctactactt tgattacaan gagcagctcc ccgagtcagc ctatatgcac
                                                                                                                                                                                                                                               300
        cagetettgg geeteaacet cetetteetg etgteecaga acegggtgge tgantnecae
                                                                                                                                                                                                                                               360
                                                                                                                                                                                                                                      420
        acgganttgg ancggctgcc tgcccaanga catacanacc aatgtctaca tcnaccacca
                                                                                                                                                                                                                                                480
        qtqtcctqqa:qcaatactga tgqanggcag ctaccncaaa gtnttcctgg:ccnagggtaa
                                                                                                                                                                                                                                               540
        cateccege egagagetae acettettea ttgacatect getegacaet ateagggatg
aaaatcgcng ggttgctcca gaaaggctnc aanaanatcc ttttcnctga aggcccccgg
                                                                                                                                                                                                                                               600
        athenetagt netagaateg geogecate geggtggane etceaacett tegttneect
                                                                                                                                                                                                                                               660
     ttactgaggg ttnattgccg cccttggcgt tatcatggtc acncengttn cctgtgttga 720
                         <210>-35;
<211> 834
<212> DNA: Seption: Cauting Control of the con
                                                                                                                                                                                                                                      756
        aattnttaac ccccacaat tccacgccna cattng
                           <213> Homo sapiena Thromas Laboration Company of the Company of th
                            <220>
                            <221> misc feature
                            <222> (1)...(834)
                            <223> n = A, T, C or G
                            <400> 35
        ggggatetet anatenacet gnatgeatgg ttgteggtgt ggtegetgte gatgaanatg
                                                                                                                                                                                                                                                  60
        aacaggatet tgecettgaa getetegget getgtnttta agttgeteag tetgeegtea
                                                                                                                                                                                                                                               120
                                                                                                                                                                                                                                               180
        tagtcagaca cnctcttggg caaaaaacan caggatntga gtcttgattt:cacctccaat
                                                                                                                                                                                                                                               240
        aatettengg getgtetget eggtgaacte gatgaenang ggeagetggt tgtgtntgat
                                                                                                                                                                                                                                               300
        aaantccanc angiteteet tggtgacete eeetteaaag ttgtteegge etteateaaa
                                                                                                                                                                                                                                               360
        cttctnnaan angannance canctttgtc gagctggnat ttgganaaca cgtcactgtt
```

```
ggaaactqat cccaaatqqt atqtcatcca tcqcctctqc tqcctqcaaa aaacttqctt
                                                                      420
ggcncaaatc cgactcccn tecttgaaag aagccnatca caccccctc cetggactcc
                                                                      480
nncaangact ctnccgctnc cccntccnng cagggttggt ggcannccgg gcccntgcgc
                                                                      540
ttcttcagcc agttcacnat nttcatcagc ccctctgcca gctgttntat tccttgggg
                                                                      600
ggaancegte tetecettee tgaannaact ttgaccgtng gaatageege genteneent
                                                                      660
achtnetggg cegggtteaa anteceteen ttgnennten cetegggeea ttetggattt
                                                                      720
nconaacttt ttoottooco encecenegg ngtttggntt tttoatnggg coccaactet
                                                                      780
getnttggcc anteceetgg gggentntan enceceetnt ggtecentng ggcc
                                                                      834
      <210> 36
      <211> 814
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (814)
      <223> n = A,T,C or G
      <400> 36
eggnegettt cengeegege eeegttteea tgacnaagge teeetteang ttaaatacnn
                                                                       60
cctagnaaac attaatgggt tgctctacta atacatcata cnaaccagta agcctgccca
                                                                      120
naacgccaac tcaggccatt cctaccaaag gaagaaaggc tggtctctcc acccctgta
                                                                      180
ggaaaggcct gccttgtaag acaccacaat ncggctgaat ctnaagtctt gtgttttact
                                                                      240
aatggaaaaa aaaaataaac aanaggtttt gttctcatgg ctgcccaccg cagcctggca
                                                                      300
ctaaaacanc ccagcgctca cttctgcttg ganaaatatt ctttgctctt ttggacatca
                                                                      360
ggcttgatgg tateactgcc acntttccac ccagctgggc necetteccc catntttgtc
                                                                      420
antganetgg aaggeetgaa nettagtete caaaagtete ngcecacaag accggecace
                                                                      480
aggggangtc ntttncagtg gatctgccaa anantacccn tatcatcnnt gaataaaaag
                                                                      540
gcccctgaac ganatgcttc cancancctt taagacccat aatcctngaa ccatggtgcc
                                                                      600
cttccggtct gatccnaaag gaatgttect gggteccant cectectttg ttnettaegt
                                                                      660
tgtnttggac centgetngn atnacecaan tganatecec ngaageacec tneecetgge
                                                                      720
atttganttt cntaaattct ctgccctacn nctgaaagca cnattccctn ggcnccnaan
                                                                      780
ggngaactca agaaggtctn ngaaaaacca cncn
                                                                      814
      <210> 37
      <211> 760
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(760)
      <223> n = A, T, C or G
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gegeagtgtt egetgaaggg gttgtagtae eagegeggga tgeteteett geagagteet 120
gtgtctggca ggtccacgca atgccctttg tcactgggga aatggatgcg ctggagctcg
                                                                      180
tenaanceae tegtgtattt tteacangea geeteeteeg aagenteegg geagttgggg
                                                                    240
gtgtcgtcac actccactaa actgtcgatn cancagccca ttgctgcagc ggaactgggt
                                                                      300
gggctgacag gtgccagaac acactggatn ggcctttcca tggaagggcc tgggggaaat
                                                                      360
encetnance caaactgeet etcaaaggee acettgeaca eccegacagg etagaaatge
                                                                      420
actettette ecaaaggtag ttgttettgt tgeecaagea neetecanea aaccaaaane
                                                                      480
ttgcaaaatc tgctccgtgg gggtcatnnn taccanggtt ggggaaanaa acccggcngn
                                                                      540
ganceneett gtttgaatge naaggnaata ateeteetgt ettgettggg tggaanagea
                                                                      600
caattgaact qttaacnttq qgccgngttc cnctnqqqtq qtctqaaact aatcaccqtc
                                                                      660
actggaaaaa ggtangtgcc ttccttgaat tcccaaantt cccctngntt tgggtnnttt
                                                                      720
```

```
760
    ctcctctncc ctaaaaatcg tnttcccccc ccntanggcg
               <210> 38
               <211> 724
               <212> DNA
               <213> Homo sapien
               <220>
               <221> misc_feature
               <222> (1) ... (724)
               <223>.n = A, T, C or G
               <400> 38
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    cttcchaat totccaacc cctcnnccaa atnnccattt ccggggggg gttccaaacc
    caaattaatt ttgganttta aattaaatnt tnattngggg aanaanccaa atgtnaagaa ...
    aatttaaccc attatnaact taaatnootn gaaaccontg gnttocaaaa atttttaacc
    cttaaatccc tccgaaattg ntaanggaaa accaaattcn cctaaggctn tttgaaggtt
    ngatttaaac ccccttnant tnttttnacc cnngnctnaa ntatttngnt tccggtgttt
                                                                                                                                     420
    tectnttaan entnggtaac teeegntaat gaannneest aanceaatta aacegaattt
    tttttgaatt ggaaatteen ngggaattna ceggggtttt tecentttgg gggeeatnee 480
    cccnctttcg gggtttgggn ntaggttgaa tttttnnang ncccaaaaaa ncccccaana .... 540
    aaaaaactcc caagnnttaa ttngaatntc ccccttccca ggccttttgg gaaaggnggg 600
    tttntggggg congggantt onttocccon ttnconccc occconggt aaanggttat 660
    ngnntttggt tittgggccc cttnanggac cttcggatn gaaattaaat ccccgggncg 720
                   รอยามองลูป (การ อากาสราก รับรวย ออกาสุดกุลวัน โดยรับสารสาร การุปนี้จากการเปลี่ย
    gccg
                            A The content of the common property of the Content of the Content
              <220> misc feature
               <221> misc feature
                                                                      , .
                                                                                   <222> (1)...(751)
               <223> n = A, T, C or G
    ttttttttt tttttctttq ctcacattta atttttattt tgatttttt taatgctgca
                                                                                                                                       60
    caacacaata tttatttcat ttgtttcttt tatttcattt tatttgtttg ctgctgctgt
                                                                                                                                     120
    tttatttatt tttactgaaa gtgagaggga acttttgtgg ccttttttcc tttttctgta
                                                                                                                                     180
    ggccgcctta agctttctaa atttggaaca tctaagcaag ctgaanggaa aagggggttt
                                                                                                                                     240
    cqcaaaatca ctcqqqqqaa nqqaaaqqtt qctttqttaa tcatqcccta tqqtqqqtga 🗅
                                                                                                                                     300
    ttaactqctt gtacaattac ntttcacttt taattaattg tgctnaangc tttaattana
                                                                                                                                     360
    cttqqqqqtt ccctcccan accaacccn ctgacaaaaa gtgccngccc tcaaatnatg
                                                                                                                                     420
    teceggennt entigaaaca eaengengaa ngiteteatt niceeenene eagginaaaa
                                                                                                                                     480
tgaagggtta ccatntttaa cnccacctcc acntggcnnn gcctgaatcc tcnaaaancn
                                                                                                                                     540
 ccctcaanch aatthctnng ccccggtchc gentnngtcc chcccggget ccgggaanth
caccconga annonntnno naacnaaatt cogaaaatat toconntono toaattocco conagactnt cotonnonan choaatttto tettnntoac gaacnognno chnaaaatgn 720
   connagacint ceremician encaatitie tetiniteae gaachegine chhaaaatgh
nnnnenecte encingteen maateneean e

<210>,40
<211>,753
<212>,DNA
<213> Homo sapien
<220>
```

```
<221> misc feature
      <222> (1) ... (753)
      \langle 223 \rangle n = A, T, C or G
      <400> 40
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                                                                       60
agatgaaaac cccccgaga cagcagcact gcaactgcca agcagccggg gtaggagggg
                                                                        120
egecetatge acagetggge cettgagaca geagggette gatgteagge tegatgteaa
                                                                        180
tggtctggaa gcggcggctg tacctgcgta ggggcacacc qtcaqqqccc accaqqaact
                                                                        240
tctcaaagtt ccaggcaacn tcgttgcgac acaccggaga ccaggtgatn agcttggggt
                                                                        300
cggtcataan cgcggtggcg tcgtcgctgg gagctggcag ggcctcccgc aggaaggcna
                                                                        360
ataaaaggtg cgcccccgca ccgttcanct cgcacttctc naanaccatg angttgggct
                                                                        420
cnaacccacc accannegg acttecttga nggaatteec aaatetette gntettggge
                                                                        480
ttetnetgat gecetanetg gttgeeengn atgecaanea neceeaanee eegggeteet
                                                                        540
aaancaccon cotcotontt toatotgggt tnttntcccc ggaccntggt toctctcaag
                                                                        600
ggancccata tctcnaccan tactcaccnt ncccccccnt gnnacccanc cttctanngn
                                                                        660
ttcccncccg nectetggcc enteaaanan gettneacna eetgggtetg cetteecee
                                                                        720
tnecetatet gnacecenen tttgtetean tnt
                                                                        753
      <210> 41
      <211> 341
      <212> DNA
      <213> Homo sapien
      <400> 41
actatateca teacaacaga catgetteat eccatagaet tettgacata getteaaatg
                                                                        60
agtgaaccca teettgattt atatacatat atgtteteag tattttggga geettteeae
                                                                       120
ttetttaaac ettgtteatt atgaacactg aaaataggaa tttgtgaaga gttaaaaagt
                                                                       180
tatagcttgt ttacgtagta agtttttgaa gtctacattc aatccagaca cttagttgag
                                                                       240
tgttaaactg tgatttttaa aaaatatcat ttgagaatat tctttcagag gtattttcat
                                                                       300
ttttactttt tgattaattg tgttttatat attagggtag t
                                                                       341
      <210> 42
      <211> 101
      <212> DNA
      <213> Homo sapien
      <400> 42
acttactgaa tttagttctg tgctcttcct tatttagtgt tgtatcataa atactttgat
                                                                        60
gtttcaaaca ttctaaataa ataattttca gtggcttcat a
                                                                       101
      <210> 43
      <211> 305
      <212> DNA
      <213> Homo sapien
      <400> 43
acatetttgt tacagtetaa gatgtgttet taaateacea tteetteetg gteeteacee
tocagggtgg totcacactg taattagage tattgaggag totttacage aaattaagat
                                                                       120
tcagatgcct tgctaagtct agagttctag agttatgttt cagaaagtct aagaaaccca
                                                                       180
cctcttgaga ggtcagtaaa gaggacttaa tatttcatat ctacaaaatg accacaggat
                                                                       240
tggatacaga acgagagtta tcctggataa ctcagagctg agtacctgcc cqqqqqcqc
                                                                       300
tcgaa
                                                                       305
                     egick a the access to the experience to the contract of the
      <210> 44
      <211> 852
      <212> DNA
      <213> Homo sapien
```

```
<220>
      <221> misc_feature
      <222> (1) ... (852)
      <223> n = A, T, C or G
      <400> 44
                                                                           60
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gattatttgg tgtgtgtttt ggtttgtgtc caaagtattg gcagcttcag ttttcatttt
                                                                          120
ctctccatcc togggcattc ttcccaaatt tatataccag tcttcgtcca tccacacgct
                                                                          180
ccagaatttc tcttttgtag taatatctca tagetcggct gagettttca taggtcatge
                                                                          240
tgctgttgtt cttctttta ccccatagct gagccactgc ctctgatttc aagaacctga
                                                                          300
agacgccctc agateggtct teccatttta ttaatectgg gttettgtct gggttcaaga
                                                                          360
ggatgtegeg gatgaattee cataagtgag teeetetegg gttgtgettt ttggtgtgge
                                                                          420
acttggcagg ggggtcttgc tccttttca tatcaggtga ctctgcaaca ggaaggtgac
                                                                          480
tggtggttgt catggagatc tgagcccggc agaaagtttt gctgtccaac aaatctactg
                                                                          540
tgctaccata gttggtgtca tataaatagt tctngtcttt ccaggtgttc atgatggaag
                                                                          600
gctcagtttg ttcagtcttg acaatgacat tgtgtgtgga ctggaacagg tcactactgc
                                                                          660
actggccgtt ccacttcaga tgctgcaagt tgctgtagag gagntgcccc gccgtccctg
                                                                          720
ccgcccgggt gaactcctgc aaactcatgc tgcaaaggtg ctcgccgttg atgtcgaact
                                                                          780
cntggaaagg gatacaattg gcatccagct ggttggtgtc caggaggtga tggagccact
                                                                          840
                                                                          852
cccacacctg gt
                                                             With the same
                                                      Barbara and Salah
      <210> 45
      <211> 234
      <212> DNA
                       และ หูเวลิต ค. เทราะ กำแหน่ง การ วิจานหารีส์และ ๑๐ การ จาก เลาการที่สินใน ๑๐
      ្សារ (ក្រុម ប្រជាជា មិន ស្រុក នេះ ខេត្ត ព្រះស្រែង ស្ថិត ស្ថិត ស្ថិត ស្ថិត ស្ថិត ស្ថិត ស្ថិត ស្ថិត ស្ថិត ស្ថិត
ស្ថិត ស្ថិត ស្ថិត ស្ថិត ស្ថិត ស្ថិត ស្ថិត ស្ថិត ស្ថិត ស្ថិត ស្ថិត ស្ថិត ស្ថិត ស្ថិត ស្ថិត ស្ថិត ស្ថិត ស្ថិត ស
acaacaqacc cttqctcqct aacqacctca tqctcatcaa gttqqacqaa tccqtqtccq
agtictgacac categogage atcagcattg ettegoagtg ecetacogog gggaactett
                                                                          120
                                                                          180
qcctcqtttc tgqctqgggt ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg
                                                                          234
tgaacqtqtc qgtqgtgtct gaggaggtct gcagtaagct ctatgacccg ctgt
      <210> 46
      <211> 590
      <212> DNA
      <213> Homo sapien
           Strain Land
      <220>
      <221> misc feature
      <222> (1)...(590)
      <223> n = A, T, C or G
      <400> 46
                                                                           60
actttttatt taaatgttta taaggcagat ctatgagaat gatagaaaac atggtgtgta
                                                                          120
atttgatagc aatattttgg agattacaga gttttagtaa ttaccaatta cacagttaaa
aagaagataa tatattocaa goanatacaa aatatotaat gaaagatoaa ggoaggaaaa
                                                                          180
tgantataac taattgacaa tggaaaatca attttaatgt gaattgcaca ttatccttta
                                                                          240
acagetteca aaanaaanaa ttattgeagt etanttaatt caaacagtgt taaatggtat
                                                                          300
caggataaan aactgaaggg canaaagaat taattttcac ttcatgtaac ncacccanat
                                                                          360
ttacaatggc ttaaatgcan ggaaaaagca gtggaagtag ggaagtantc aaggtctttc
                                                                          420
togtetetaa tetgeettae tetttgggtg tggetttgat eetetggaga eagetgeeag
                                                                          480
                                                                          540
ggctcctgtt atatccacaa tcccagcagc aagatgaagg gatgaaaaag gacacatgct
gccttccttt gaggagactt catctcactg gccaacactc agtcacatgt
                                                               37 37 LON
      <210> 47
                                                               10 c.
      <211> 774
                                                         English Good (Control
```

```
<212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(774)
      <223> n = A, T, C or G
      <400> 47
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                                                                       60
tgaacagaat tttcctgnac aacggggctt caaaataatt ttcttgggga ggttcaagac
                                                                      120
getteactge ttgaaactta aatggatgtg ggacanaatt ttetgtaatg accetgaggg
                                                                      180
cattacagac gggactctgg gaggaaggat aaacagaaag gggacaaagg ctaatcccaa
                                                                      240
aacatcaaag aaaggaaggt ggcgtcatac ctcccagcct acacagttct ccagggctct
                                                                      300
cctcatccct qqaqqacqac aqtqqaqqaa caactqacca tqtccccaqq ctcctqtqtq
                                                                      360
ctggctcctg gtcttcagcc cccagctctg gaagcccacc ctctgctgat cctgcgtggc
                                                                      420
ccacactect tgaacacaca tecceaggit atattectgg acatggetga acetectatt
                                                                      480
cctacttecg agatgccttg ctccctgcag cctgtcaaaa tcccactcac cctccaaacc
                                                                      540
acggcatggg aagcctttct gacttgcctg attactccag catcttggaa caatccttga
                                                                      600
ttccccactc cttagaggca agatagggtg gttaagagta gggctggacc acttggagcc
                                                                      660
aggetgetgg cttcaaattn tggeteattt acgagetatg ggacettggg caagtnatet
                                                                      720
tcacttctat gggcntcatt ttgttctacc tgcaaaatgg gggataataa tagt
                                                                      774
      <210> 48
      <211> 124
      <212> DNA
      <213> Homo sapien <220>
       misc feature
<222> (1)...(124)
<223> n = A.T.C
canaaattga aattttataa aaaggcattt ttctcttata tccataaaat gatataattt
                                                                       60
ttgcaantat anaaatgtgt cataaattat aatgttcctt aattacagct caacgcaact
                                                                      120
tggt
                                                                      124
      <210> 49
      <211> 147
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (147)
      <223> n = A, T, C or G
      <400> 49
gccgatgcta ctattttatt gcaggaggtg ggggtgtttt tattattctc tcaacacctt
tgtggctaca ggtggtgtct gactgcatna aaaanttttt tacgggtgat tgcaaaaatt
ttagggcacc catateccaa gcantgt
                                                                      147
      <210> 50
     <211> 107
                    And the second of the second of the
      <212> DNA
     <213> Homo sapien
```

```
<400> 50
 acattaaatt aataaaagga ctgttggggt tctgctaaaa cacatggctt gatatattgc
                                                                                                                                                                                                                        60
 atggtttgag gttaggagga gttaggcata tgttttggga gaggggt
                                                                                                                                                                                                                     107
                   <210> 51
                   <211> 204
                   <212> DNA
                  <213> Homo sapien
                  <400> 51
 gtcctaggaa gtctagggga cacacgactc tggggtcacg gggccgacac acttgcacgg 60
                                                                                                                                         A 4 4 4 4 4 4 4 5
 cgggaaggaa aggcagagaa gtgacaccgt cagggggaaa tgacagaaag gaaaatcaag 120
gccttgcaag gtcagaaagg ggactcaggg cttccaccac agccctgccc cacttggcca
cctccctttt gggaccagca atgt

<210> 52

<211> 491

<212> DNA

<213> Homo sapien
                  <220>

<221> misc_feature
                  <222> (1)...(491)
                  <223> n = A, T, C or G
                  <400> 52
 acaaagataa catttatctt ataacaaaaa tttgatagtt ttaaaggtta gtattgtgta
 gggtattttc caaaagacta aagagataac tcaggtaaaa agttagaaat gtataaaaca
                                                                                                                                                                                                                     120
 ccatcagaca ggtttttaaa aaacaacata ttacaaaatt agacaatcat ccttaaaaaa
                                                                                                                                                                                                                     180
 aaaacttctt gtatcaattt cttttgttca aaatgactga cttaantatt tttaaatatt
                                                                                                                                                                                                                     240
 tcanaaacac ttcctcaaaa attttcaana tggtagcttt canatgtncc ctcagtccca
                                                                                                                                                                                                                    300
atgttgctca gataaataaa tctcgtgaga acttaccacc caccacaagc tttctggggc
                                                                                                                                                                                                                    360
 atgcaacagt gtcttttctt tnctttttct ttttttttt ttacaggcac agaaactcat
                                                                                                                                                                                                                     420
 caattttatt tggataacaa agggtctcca aattatattg aaaaataaat ccaagttaat
                                                                                                                                                                                                                     480
atcactcttg to the second and the second at t
                                                             and electronic models of the control of the control
                  <210> 53
                  <211> 484
                  <212> DNA
                  <213> Homo sapien
                  <220>
                  <221> misc_feature
                  <222> (1)...(484)
                  <223> n = A, T, C or G
                  <400> 53
 acataattta gcagggctaa ttaccataag atgctattta ttaanaggtn tatgatctga
                                                                                                                                                                                                                       60
gtattaacag ttgctgaagt ttggtatttt tatgcagcat tttctttttg ctttgataac
                                                                                                                                                                                                                    120
actacagaac cottaaggac actgaaaatt agtaagtaaa gttcagaaac attagctgct
                                                                                                                                                                                                                    180
caatcaaatc tctacataac actatagtaa ttaaaacgtt aaaaaaaagt gttgaaatct
                                                                                                                                                                                                                    240
gcactagtat anaccgctcc tgtcaggata anactgcttt ggaacagaaa gggaaaaanc
                                                                                                                                                                                                                    300
agetttgant ttetttgtge tgatangagg aaaggetgaa ttacettgtt geeteteect
                                                                                                                                                                                                                    360
aatgattggc aggtcnggta aatnccaaaa catattccaa ctcaacactt cttttccncg
                                                                                                                                                                                                                    420
tancttgant ctgtgtattc caggancagg cggatggaat gggccagccc ncggatgttc
                                                                                                                                                                                                                    480
                                                                                                                                                                                                                    484
cant
                                                                                                                                                                                350 SEE
                                                                                                                                                         Deligno thick (EI).
```

<210> 54

| <211> 151<br><212> DNA<br><213> Homo sapien                                                                            | 1                                     |            |                                                                              |                  |
|------------------------------------------------------------------------------------------------------------------------|---------------------------------------|------------|------------------------------------------------------------------------------|------------------|
| <400> 54  actaaacete gtgettgtga actecate ceactgggta tactgetgae aacegeae tetatgteet eteaagtgee tttttgt                  | aca acaaaaacac                        |            |                                                                              | 60<br>120<br>151 |
| <210> 55<br><211> 91<br><212> DNA<br><213> Homo sapien                                                                 | e e e e e e e e e e e e e e e e e e e |            |                                                                              | , · · · ·        |
| <pre>&lt;400&gt; 55 acctggcttg teteegggtg gtteeeg gccetecagt ggataetega gecaaag</pre>                                  |                                       | tccccagaac | ggacactttc                                                                   | 60<br>91         |
| <210> 56<br><211> 133<br><212> DNA<br><213> Homo sapien                                                                | •                                     | e e        |                                                                              |                  |
| <pre>&lt;400&gt; 56 ggcggatgtg cgttggttat atacaaa tggatttttg gtatctgtgg gttggggg aagggacaac tgt</pre>                  |                                       |            |                                                                              | 60<br>120<br>133 |
| <210> 57<br><211> 147<br><212> DNA<br><213> Homo sapien                                                                |                                       |            |                                                                              |                  |
| <220> <221> misc_feature <222> (1)(147) <223> n = A,T,C or G                                                           |                                       | •          |                                                                              | · '              |
| <400> 57 actctggaga acctgagccg ctgctccg gactgggagc tgagcccttc cctttgcg tctcantggg ctggatncat gcagggt                   |                                       |            |                                                                              | 60<br>120<br>147 |
| <210> 58<br><211> 198<br><212> DNA<br><213> Homo sapien                                                                |                                       | * . *      | 9 .4<br>.4 k /2<br>.7 k .4 k .2 k<br>.7 k .4 k |                  |
| <220> <221> misc_feature <222> (1)(198) <223> n = A,T,C or G                                                           |                                       |            | · · · · · · · · · · · · · · · · · · ·                                        |                  |
| <pre>&lt;400&gt; 58 acagggatat aggtttnaag ttattgtr tgattacata catttatcct ttaaaaaa atttaccaat gagttacctt gtaaatga</pre> | aga tgtaaatctt                        | aatttttatg | ccatctatta                                                                   | 60<br>120<br>180 |

| <210> 59<br><211> 330<br><212> DNA<br><213> Homo sapid                                                                                                        | e <b>n</b>                                           | ·                                      |                                                                                                                 |                                        |                    |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------|----------------------------------------|-----------------------------------------------------------------------------------------------------------------|----------------------------------------|--------------------|
| <pre>&lt;400&gt; 59 acaacaaatg ggttgtgagg ccattgaaaa ttatcattaa cacctgtgct agcttgctaa tacagtcaat aaatgacaaa cagaaggaat ctattttatc tttcgtcttt attggacttc</pre> | tgattttaaa<br>aatgggagtt<br>gccagggcct<br>acatggatct | tgacaagtta<br>aactctagag<br>acaggtggtt | tcaaaaactc<br>caaatatagt<br>tccagacttt                                                                          | actcaatttt<br>atcttctgaa<br>ccagacccag | 120<br>180<br>1240 |
| <210> 60<br><211> 175<br><212> DNA<br><213> Homo sapid                                                                                                        | en ,                                                 |                                        |                                                                                                                 |                                        |                    |
| <400> 60<br>accgtgggtg cettetacat<br>gtegtggget cetteetett<br>teetggaace ageggtgget                                                                           | catcctcatc                                           | cagctggtgc                             | tgctcatcga                                                                                                      | ctttgcgcac                             |                    |
| <210> 61<br><211> 154<br><212> DNA<br><213> Homo sapie                                                                                                        | ∍n                                                   | e da Silva da A                        | er i State de la composition de la comp |                                        |                    |
| <400> 61<br>accccacttt tcctcctgtg<br>ggttgttgct cttcaacagt<br>tggactgcac agccccgggg                                                                           | atcctcccct                                           | ttccggatct                             | gctacatgat<br>gctgagccgg                                                                                        | gagggtgagt<br>acagcagtgc               | 60<br>120<br>154   |
| <210> 62<br><211> 30<br><212> DNA<br><213> Homo sapie                                                                                                         | en                                                   |                                        |                                                                                                                 |                                        | • •                |
| <400> 62<br>egetegagee etatagtgag                                                                                                                             | tcgtattaga                                           |                                        |                                                                                                                 |                                        | 30                 |
| <210> 63<br><211> 89<br><212> DNA<br><213> Homo sapie                                                                                                         | en.                                                  |                                        |                                                                                                                 |                                        |                    |
| <400> 63<br>acaagtcatt tcagcaccct<br>ctgtatgaat aaaaatggtt                                                                                                    |                                                      | aaactgacca                             | tctttatat                                                                                                       | ttaatgcttc                             | 60<br>89           |
| <210> 64<br><211> 97<br><212> DNA                                                                                                                             | •                                                    | • 1                                    |                                                                                                                 |                                        |                    |
| <213> Homo sapie<br><400> 64<br>accggagtaa ctgagtcggg                                                                                                         |                                                      | 12.                                    | aataaataaa                                                                                                      | යන්න යන්මය                             | strings "the       |

| aatcagtgca tccaggattg gtccttggat ctggggt                                                                                                                                                                                                                                                                                                                                                                                                                          | 97,                                          |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|
| <210> 65<br><211> 377<br><212> DNA<br><213> Homo sapien                                                                                                                                                                                                                                                                                                                                                                                                           |                                              |
| <220> <221> misc_feature <222> (1)(377) <223> n = A,T,C or G                                                                                                                                                                                                                                                                                                                                                                                                      |                                              |
| <pre>&lt;400&gt; 65 acaacaanaa ntcccttctt taggccactg atggaaacct ggaaccccct tttgatggca gcatggcgtc ctaggccttg acacagcggc tggggtttgg gctntcccaa accgcacacc ccaaccctgg tctacccaca nttctggcta tgggctgtct ctgccactga acatcagggt tcggtcataa natgaaatcc caanggggac agaggtcagt agaggaagct caatgagaaa ggtgctgttt gctcagccag aaaacagctg cctggcattc gccgctgaac tatgaacccg tgggggtgaa ctacccccan gaggaatcat gcctgggcga tgcaanggtg ccaacaggag gggcgggagg agcatgt</pre>          | 60<br>120<br>180<br>240<br>300<br>360<br>377 |
| <210> 66<br><211> 305<br><212> DNA<br><213> Homo sapien                                                                                                                                                                                                                                                                                                                                                                                                           |                                              |
| <pre>&lt;400&gt; 66 acgcctttcc ctcagaattc agggaagaga ctgtcgcctg ccttcctccg ttgttgcgtg agaacccgtg tgccccttcc caccatatcc accctcgctc catctttgaa ctcaaacacg aggaactaac tgcaccctgg tcctctcccc agtccccagt tcaccctcca tccctcacct tcctccactc taagggatat caacactgcc cagcacaggg gccctgaatt tatgtggttt ttatatattt tttaataaga tgcactttat gtcattttt aataaagtct gaagaattac</pre>                                                                                                | 60<br>120<br>180<br>240<br>300               |
| <pre>tgttt  &lt;210&gt; 67 &lt;211&gt; 385 &lt;212&gt; DNA &lt;213&gt; Homo sapien</pre>                                                                                                                                                                                                                                                                                                                                                                          | 305                                          |
| <pre>&lt;400&gt; 67 actacacaca ctccacttgc ccttgtgaga cactttgtcc cagcacttta ggaatgctga ggtcggacca gccacatctc atgtgcaaga ttgcccagca gacatcaggt ctgagagttc cccttttaaa aaaggggact tgcttaaaaa agaagtctag ccacgattgt gtagagcagc tgtgctgtgc tggagattca cttttgagag agttctcctc tgagacctga tctttagagg ctgggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgcttg cctctcccag ggccccagcc tggccacacc tgcttacagg gcactctcag atgcccatac catagtttct gtgctagtgg accgt</pre> | 60<br>120<br>180<br>240<br>300<br>360<br>385 |
| <210> 68 <211> 73 <212> DNA <213> Homo sapien                                                                                                                                                                                                                                                                                                                                                                                                                     |                                              |
| <400> 68 acttaaccag atatatttt accccagatg gggatattct ttgtaaaaaa tgaaaataaa gttttttaa tgg                                                                                                                                                                                                                                                                                                                                                                           | 60<br>73                                     |
| <210> 69                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                              |

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<211> 536
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        <213> Homo sapien
        <220>
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        <223> n = A,T,C or G
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  actagtccag tgtggtggaa ttccattgtg ttgggggctc tcaccetect ctcctgcage
                                                                      60
  tocagetttg tgetetgeet etgaggagae catggeecag catetgagta ecetgetget
                                                                     120
  cctgctggcc accctagctg tggccctggc ctggagcccc aaggaggagg ataggataat
                                                                     180
  cccgggtggc atctataacg cagacctcaa tgatgagtgg gtacagcgtg cccttcactt
                                                                    240
  cgccatcagc gagtataaca aggccaccaa agatgactac tacagacgtc cgctgcgggt
  actaagagcc aggcaacaga ccgttggggg ggtgaattac ttcttcgacg tagaggtggg 10 360
-- ccgaaccata tgtaccaagt cccagccaa cttggacacc tgtgccttcc atgaacagcc 420
  agaactgcag aagaaacagt tgtgctcttt cgagatctac gaagttccct ggggagaaca 480
  gaangtccct gggtgaaatc caggtgtcaa gaaatcctan ggatctgttg ccaggc
       <210> 70"
       <211> 477
       <212> DNA
       <213> Homo sapien
  <400> 70
  atgaccccta acaggggccc tctcagccct cctaatgacc tccggcctag ccatgtgatt ...
  tcacttccac tccataacgc tcctcatact aggcctacta accaacacac taaccatata 120
  ccaatgatgg cgcgatgtaa cacgagaaag cacataccaa ggccaccaca caccacctgt 180
  ccaaaaaggc cttcgatacg ggataatcct atttattacc tcagaagttt ttttcttcgc
  agggattttt ctgagccttt taccactcca gcctagcccc tacccccaa ctaggagggc
                                                                    300
  actggcccc aacaggcatc accccgctaa atcccctaga agtcccactc ctaaacacat
                                                                    360
  ccgtattact cgcatcagga gtatcaatca cctgagctca ccatagtcta atagaaaaca
                                                                    420
  accgaaacca aattattcaa agcactgctt attacaattt tactgggtct ctatttt
                                                                    477
       <210> 71
       <211> 533
       <212> DNA
       <213> Homo sapien
       <221> misc_feature
                               eren oblik
1804. – Sistem
       agagetatag gtacagtgtg ateteagett tgcaaacaca ttttetacat agatagtact
                                                                    . 60
 aggtattaat agatatgtaa agaaagaaat cacaccatta ataatggtaa gattggttta
                                                                    120
 tgtgatttta gtggtatttt tggcaccctt atatatgttt tccaaacttt cagcagtgat
                                                                    180
 attatttcca taacttaaaa agtgagtttg aaaaagaaaa tctccagcaa gcatctcatt
                                                                    240
 taaataaagg tttgtcatct ttaaaaatac agcaatatgt gactttttaa aaaagctgtc
                                                                    300
 aaataggtgt gaccctacta ataattatta gaaatacatt taaaaaacatc gagtacctca
                                                                    360
 agtcagtttg ccttgaaaaa tatcaaatat aactcttaga gaaatgtaca taaaagaatg
 cttcgtaatt ttggagtang aggttccctc ctcaattttg tatttttaaa aagtacatgg 480
 taaaaaaaaa aattcacaac agtatataag gctgtaaaat gaagaattct.gcc
                                                           ្នុងរាជ សុវៈមិន ១១១
       <210> 72
```

<211> 511

```
<212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
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      <400> 72
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aaatgaaagg cttccaggca gttatctgat taaagaacac taaaagaggg acaaggctaa
                                                                    120
aagccgcagg atgtctacac tatancaggc gctatttggg ttggctggag gagctgtgga
                                                                    180
aaacatggan agattggtgc tgganatcgc cgtggctatt cctcattgtt attacanagt
                                                                    240
gaggttctct gtgtgcccac tggtttgaaa accgttctnc aataatgata gaatagtaca
                                                                    300
cacatgagaa ctgaaatggc ccaaacccag aaagaaagcc caactagatc ctcagaanac
                                                                    360
gcttctaggg acaataaccg atgaagaaaa gatggcctcc ttgtgccccc gtctgttatg
                                                                    420
                                                                    480
atttctctcc attgcagcna naaacccgtt cttctaagca aacncaggtg atgatggcna
                                   _ _____ acyacygen
                                                                    511
aaatacaccc cctcttgaag naccnggagg a
               talin in the second second
      <210> 73
      <211> 499
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(499)
      <223> n = A, T, C or G
      <400> 73
cagtgccagc actggtgcca gtaccagtac caataacagt gccagtgcca gtgccagcac
cagtggtggc ttcagtgctg gtgccagcct gaccgccact ctcacatttg ggctcttcgc
                                                                    120
tggccttggt ggagctggtg ccagcaccag tggcagctct ggtgcctgtg gtttctccta
                                                                    180
                                                                    240
caaqtqaqat tttaqatatt gttaatcctg ccagtctttc tcttcaagcc agggtgcatc
ctcagaaacc tactcaacac agcactctag gcagccacta tcaatcaatt gaagttgaca
420
antitagagg gecegtttaa accegetgat cageetegae tgtgeettet anttgecage
catctgttgt ttgcccctcc cccgntgcct tccttgaccc tggaaagtgc cactcccact
                                                                    480
                                                                    499
gtcctttcct aantaaaat
                                <210> 74
      <211> 537
      <212> DNA
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      <220>
      <221> misc_feature
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      <400> 74
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                                                                   60
                                                                    120
ttatcagctt aactcagata aaatcattga aagtaataag gtaaaagcta gtctctaact
                                                                    180
tccaggccca cggctcaagt gaatttgaat actgcattta cagtgtagag taacacataa
cattgtatgc atggaaacat ggaggaacag tattacagtg tectaccact ctaatcaaga
                                                                    240
aaagaattac agactctgat tctacagtga tgattgaatt ctaaaaatgg taatcattag
                                                                    300
ggcttttgat ttataanact ttgggtactt atactaaatt atggtagtta tactgccttc
                                                                    360
cagtttgctt gatatatttg ttgatattaa gattcttgac ttatattttg aatgggttct
                                                                    420
```

actgaaaaan gaatgatata ttcttgaaga catcgatata catttattta cactcttgat 480

```
tctacaatgt agaaaatgaa ggaaatgccc caaattgtat ggtgataaaa gtcccqt
                                          <210> 75
                                          <211> 467
                                          <212> DNA
                                           <213> Homo sapien
                                         <220>
                                                                                                                                                                                                                                 n de la companya de l
                                         <221> misc_feature <222> (1)...(467)
                                                                                                                                                                                                              And the state of the state of
                                           <223> n = A, T, C \text{ or } G

    And the state of t
                                          <400> 75
      caaanacaat tgttcaaaag atgcaaatga tacactactg ctgcagctca caaacacctc
tgcatattac acgtacetec tectgetect caagtagtgt ggtetatttt gecateatea 120
cctgctgtct gcttagaaga acggctttct gctgcaangg agagaaatca taacagacgg 180
          tggcacaagg aggccatctt ttcctcatcg gttattgtcc ctagaagcgt cttctgagga
                                                                                                                                                                                                                                                                                                                                                                                 240
          totagttggg ctttctttct gggtttgggc catttcantt ctcatgtgtg tactattcta
                                                                                                                                                                                                                                                                                                                                                                                  300
          tcattattgt ataacggttt tcaaaccngt gggcacncag agaacctcac tctgtaataa
                                                                                                                                                                                                                                                                                                                                                                                  360
          caatgaggaa tagccacggt gatctccagc accaaatctc tccatgttnt tccagagctc
                                                                                                                                                                                                                                                                                                                                                                                  420
          ctccaqccaa cccaaatagc cgctgctatn gtgtagaaca tccctgn
                                                                                                                                                                                                                                                                                                                                                                                   467
                                        <210> 76
                                         <211> 400
                                         <212> DNA
                                         <213> Homo sapien
                                         <220>
                                         <221> misc feature
                                         <222> (1)...(400)
                                         \langle 223 \rangle n = A,T,C or G
                                         <400> 76
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         tetetettte tggcetggag getatecage gtactecaaa gatteaggtt tacteaegte
                                                                                                                                                                                                                                                                                                                                                                                  120
atccagcaga gaatggaaag tcaaatttcc tgaattgcta tgtgtctggg tttcatccat
                                                                                                                                                                                                                                                                                                                                                                                  180
         ccgacattga agttgactta ctgaagaatg gagagagaat tgaaaaagtg gagcattcag
                                                                                                                                                                                                                                                                                                                                                                                  240
          acttgtcttt cagcaaggac tggtctttct atctcttgta ctacactgaa ttcacccca
                                                                                                                                                                                                                                                                                                                                                                                  300
         ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaagatng
                                                                                                                                                                                                                                                                                                                                                                                  360
         ttnagtggga tcganacatg taagcagcan catgggaggt
                                                                                                                                                                                                                                                                                                                                                                                  400
                                         <210> 77
                                         <211> 248
                                         <212> DNA
                                         <213> Homo sapien
                                         <400> 77
         ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct
                                                                                                                                                                                                                                                                                                                                                                                      60
         ccagctgecc cggcggggga tgcgaggetc ggagcaccct tgcccggctg tgattgctgc
                                                                                                                                                                                                                                                                                                                                                                                  120
         caggiaction teating teating the cattering teating the cattering teating the cattering teating 
                                                                                                                                                                                                                                                                                                                                                                                  180
         gttcatatct: ggagcctgat: gtcttaacga: ataaaggtcc:catgctccac, ccgaaaaaaa
                                                                                                                                                                                                                                                                                                                                                                                240
         aaaaaaaa 1 ee fu too is moe us shu qaalasugo si agnibbi toh si nacqiii linkii h
                                      **Comparison of the same parameters of the
                                        <213> Homo sapien/ to the appropriate Agreement to the
```

```
actagtocag tgtggtggaa ttccattgtg ttgggcccaa cacaatggct acctttaaca
tcacccagac cccgccctgc ccgtgcccca cgctgctgct aacgacagta tgatgcttac 120
tctgctactc ggaaactatt tttatgtaat taatgtatgc tttcttgttt ataaatgcct
gatttaaaaa aaaaaaaaaa a
                                                                     201
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      <211> 552
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      <220>
      <221> misc_feature
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tttaggcagt getagtaatt teetegtaat gattetgtta ttaettteet attetttatt
                                                                     120
cctctttctt ctgaagatta atgaagttga aaattgaggt ggataaatac aaaaaggtag
                                                                     180
tgtgatagta taagtatcta agtgcagatg aaagtgtgtt atatatatcc attcaaaatt
                                                                     240
atgcaagtta gtaattactc agggttaact aaattacttt aatatgctgt tgaacctact
                                                                  300
ctgttccttg gctagaaaaa attataaaca ggactttgtt agtttgggaa gccaaattga
                                                                     360
taatattota tgttotaaaa gttgggotat acataaanta tnaagaaata tggaatttta
                                                                     420
ttcccaggaa tatggggttc atttatgaat antacccggg anagaagttt tgantnaaac
                                                                     480
cngttttggt taatacgtta atatgtcctn aatnaacaag gcntgactta tttccaaaaa
                                                                     540
aaaaaaaaa aa
                                                                     552
      <210> 80
      <211> 476
      <212> DNA
    <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (476)
      <223> n = A, T, C or G
      <400> 80
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ggggaaaatg gggcctagaa gttacagagc atctagctgg tgcgctggca cccctggcct 120
cacacagact cccgagtagc tgggactaca ggcacacagt cactgaagca ggccctgttt 180
gcaattcacg ttgccacctc caacttaaac attcttcata tgtgatgtcc ttagtcacta 240
aggttaaact ttcccacca gaaaaggcaa cttagataaa atcttagagt actttcatac in 300
tettetaagt cetettecag ceteactitg agtecteett gggggttgat aggaantnite (2003) 360
tottggettt eteaataaaa tetetateea teteatgttt aatttggtac gentaaaaat
                                                                     420
gctgaaaaaa ttaaaatgtt ctgqtttcnc tttaaaaaaa aaaaaaaaaa aaaaaa
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      <211> 232
      <212> DNA
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      <220>
      <221> misc_feature
      <222> (1)...(232)
      \langle 223 \rangle n = A,T,C or G
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```
<400> 81
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                                                                                                                                                                                                                                            - 60
                                                                                                                                                                                                                                             120
         ttettetata tetttettt etggggate tteetggete tgeceeteea tteecageet
                                                                                                                                                                                                                                           180
ctcatcccca tettgcactt ttgctagggt tggaggcgct ttcctggtag cccctcagag
                                                                                                                                                                                                                                             232
          actcagtcag cgggaataag tcctaggggt ggggggtgtg gcaagccggc ct
                            <210> 82
                            <211> 383
                             <212> DNA
                            <213> Homo sapien
                                                                    1
                            <220>
                            <221> misc_feature
                          *<222> '(1) ... (383)
                            <223> n = A,T,C or G
                            <400> 82
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          agtaccagta ccaataacat gccagtgcca gtgccagcac cagtggtggc ttcagtgctg 120
          gtgccagcct gaccgccact ctcacatttg ggctcttcgc tggccttggt ggagctggtg 180
          ccagcaccag tggcagctct ggtgcctgtg gtttctccta caagtgagat tttagatatt : 240
          gttaatcctg ccagtctttc tcttcaagcc agggtgcatc ctcagaaacc tactcaacac 300
          ageactetng geagecacta teaateaatt gaagttgaca etetgeatta aatetatttg 360
         ccatttcaaa aaaaaaaaaaa aaa ori soomat tuus artoja ug Aaa or rijit 17383

oo yoo an por rodhe or bo goomat las aaa at in oo see o in in oo see oo in oo see o
                            <211> 494
                             <212> DNA
                             <213> Homo sapien
                            <220>
                             <221> misc feature
                             <222> (1)...(494)
                             <223> n = A, T, C or G
                             <400> 83
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                                                                                                                                                                                                                                                60
          gggagatcga gtctatacgc tgaagaaatt tgacccgatg ggacaacaga cctgctcagc
                                                                                                                                                                                                                                             120
          ccatcctgct cggttctccc cagatgacaa atactctcga caccgaatca ccatcaagaa
                                                                                                                                                                                                                                             180
   accettcaag gtgctcatga cecagcaacc gcgccctgtc ctctgagggt cettaaactg
                                                                                                                                                                                                                                             240
          atgtetttte tgccacetgt tacccetegg agacteegta accaaactet teggactgtg
                                                                                                                                                                                                                                             300
          agccctgatg cctttttgcc agccatactc tttggcntcc agtctctcgt ggcgattgat
                                                                                                                                                                                                                                             360
          tatgcttgtg tgaggcaatc atggtggcat cacccatnaa gggaacacat ttganttttt
                                                                                                                                                                                                                                             420
                                                                                                                                                                                                                                             480
   tttcncatat tttaaattac naccagaata nttcagaata aatgaattga aaaactctta
                                                                                                                                                                                                                                             494
  ്ട്ട-aaaaaaaaaa, aaaa, പ്രദ്യേശ്യന് നില്ലാ
                            16.0 + 2.5 = 2000; 2.0 day 2.0 day 3.0 day 3.0
  AND THE
                             <211> 380
                             <212> DNA
                             <213> Homo sapien
                            <220>
                             <221> misc_feature
                             <222> (1)...(380)
                             <223> n = A, T, C or G
                            <400> 84
```

gctggtagcc tatggcgtgg ccacggangg gctcctgagg cacgggacag tgacttccca

```
agtatectge geogegtett ctacegtece tacetgeaga tettegggea gattececag
                                                                    120
gaggacatgg acgtggccct catggagcac agcaactgct cgtcggagcc cggcttctgg
                                                                    180
gcacaccete etggggecca ggegggeace tgegtetece agtatgecaa etggetggtg
gtgctgctcc tcgtcatctt cctgctcgtg gccaacatcc tgctggtcac ttgctcattg
ccatgttcag ttacacattc ggcaaagtac agggcaacag cnatctctac tgggaaggcc
                                                                    360
agcgttnccg cctcatccgg
                                                                    380
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      <211> 481
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (481)
      <223> n = A, T, C or G
      <400> 85
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                                                                    120
ggaaactete aatcaagtea cegtenatna aacetgtgge tggttetgte tteegetegg
                                                                    180
tgtgaaagga tctccagaag gagtgctcga tcttccccac acttttgatg actttattga
                                                                    240
gtcgattctg catgtccagc aggaggttgt accagctctc tgacagtgag gtcaccagcc
                                                                   . 300
ctatcatgcc nttgaacgtg ccgaagaaca ccgagccttg tgtggggggt gnagtctcac
                                                                    360
ccagattctg cattaccaga nagccgtggc aaaaganatt gacaactcgc ccaggnngaa
                                                                   420
aaagaacacc teetggaagt getngeeget eetegteent tggtggnnge gentneettt
                                                                   480
                     and the second
                                                                    481
      <210> 86
      <211> 472
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
     <222> (1) ... (472)
      <223> n = A, T, C or G
     <400> 86
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acttggaaaa gcaacttnaa gcctggacac tggtattaaa attcacaata tgcaacactt
taaacagtgt gtcaatctgc tcccttactt tgtcatcacc agtctgggaa taagggtatg 180
ccctattcac acctgttaaa agggcgctaa gcatttttga ttcaacatct tttttttga 240,
cacaagtccg aaaaaagcaa aagtaaacag ttnttaattt gttagccaat tcactttctt 0905 300
catgggacag agccatttga tttaaaaagc aaattgcata atattgagct ttgggagctg 360
ataintgage ggaagantag cetttetaet teaceagaea caacteettt cataitggga 420:
tgttnacnaa agttatgtct cttacagatg ggatgctttt gtggcaattc tg 472
                                 90 - 1977 to 10 20 866 9
     <210> 87
     <211> 413
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc feature
     <222> (1)...(413)
     <223> n = A, T, C or G
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<400> 87

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agaaaccagt atctctnaaa acaacctctc ataccttgtg gacctaattt tgtgtgcgtg
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     tgtgtgtgcg cgcatattat atagacaggc acatcttttt tacttttgta aaagcttatg
                                                                                                                                                                                                                 120
cctctttggt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct
                                                                                                                                                                                                                 180
ttgtcttctg tgtaaatggt actagagaaa acacctatnt tatgagtcaa tctagttngt
                                                                                                                                                                                                                 240
     tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc cttgactagg
                                                                                                                                                                                                                 300
    ggggacaaag aaaagcanaa ctgaacatna gaaacaattn cctggtgaga aattncataa acagaaattg ggtngtatat tgaaananng catcattnaa acgtttttt ttt
                                                                                                                                                                                                                 360
                                                                                                                                                                                                                 413
                                                                                                                                                               一下 工具等的 法系统
                      <210> 88
                                                                                                                                                           Section Add the
                      <211> 448
                      <212> DNA
                      <213> Homo sapien
                      <220>
                      <221> misc feature
                      <222> (1)...(448)
                       <223> n = A, T, C or G
                      400>88: A TOTAL STATE OF THE STATE OF THE
     cgcagcgggt cetetetate tagetecage etetegeetg ecceaetece egegtecege 60
     gtectageen accatggeeg ggeeectgeg egeeegetg etectgetgg ecatectgge 120
     cgtggccctg gccgtgagcc ccgcggccgg ctccagtccc ggcaagccgc cgcgcctggt 180
     gggaggccca tggaccccgc gtggaagaag aaggtgtgcg gcgtgcactg gactttgccg 240
     teggenanta caacaaacce gcaacnactt ttaccnagen egegetgeag gttgtgeege
     cccaancaaa ttgttactng gggtaantaa ttcttggaag ttgaacctgg gccaaacnng 360
     tttaccagaa ccnagccaat tngaacaatt ncccctccat aacagcccct tttaaaaaagg
                                                                                                                                                                                                                420
                                                                                                                                                                                                                 448
     gaancantcc tgntcttttc caaatttt
                                                                                                                                                                                   13
                                                                                                                                                                                31 2 - 1 - 3 -
                      <210> 89
                                                                                                                                                                                7.30 18.3
                      <211> 463
                       <212> DNA
                       <213> Homo sapien
                      <220>
                       <221> misc_feature
                                                                                                                                                                                   . . . .
                       <222> (1)...(463)
                      <223> n = A, T, C or G
                      <400> 89° 1 * 1 1 2 No. 12 1 No. 14 No. 15 N
     gaattttgtg cactggccac tgtgatggaa ccattgggcc aggatgcttt gagtttatca
                                                                                                                                                                                                                 120
     qtaqtqattc tqccaaagtt ggtgttgtaa catgagtatg taaaatgtca aaaaattagc
    agaggtctag gtctgcatat cagcagacag tttgtccgtg tattttgtag ccttgaagtt
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 attinatgttm agacttgcct ctntnaaatt gcttttgtnt tctgcaggta ctatctgtgg
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  _aattetetee ccatannaaaaacccangeee ttggganaat ttgaaaaang gnteettenn
                                                                                                                                                                                                                 420
                                                                                                                                                                                                                 463
     aattonnana anttoagntn toatacaaca naacngganc ccc
                                                                                                                                                                                 The Sales
                      <210> 90
                                                                                                                                                                                 1941 175
                      <211> 400
                                                                                                                                                      amodition and their
                       <212> DNA
                      <213> Homo sapien
                                                                                                                                                     and spanish or a filesta
                      <220>
                                                                                                                                                      (2) (4) (3) (4) (4) (5)
                      <221> misc feature
                                                                                                                                                a to the part of the
                      <222> (1)...(400)
```

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\langle 223 \rangle n = A,T,C or G
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                                                                        60
cttccactca ctgtctgtaa gcntnttaac ccagactgta tcttcataaa tagaacaaat
                                                                       120
tetteaceag teacatette taggacettt ttggatteag ttagtataag etettecaet
                                                                       180
tcctttgtta agacttcatc tggtaaagtc ttaagttttg tagaaaggaa tttaattgct
                                                                       240
cgttctctaa caatgtcctc tccttgaagt atttggctga acaacccacc tnaagtccct
                                                                       300
ttgtgcatcc attttaaata tacttaatag ggcattggtn cactaggtta aattctgcaa
                                                                       360
gagtcatctg tctgcaaaag ttgcgttagt atatctgcca
                                                                       400
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      <211> 480
      <212> DNA
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      <221> misc_feature
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                                                                       120
atgeetettt gaetaeegtg tgeeagtget ggtgattete acacacetee nneegetett
                                                                       180
tgtggaaaaa ctggcacttg nctggaacta gcaagacatc acttacaaat tcacccacga
                                                                       240
gacacttgaa aggtgtaaca aagcgactct tgcattgctt tttgtccctc cggcaccagt
                                                                       300
tgtcaatact aaccegetgg tttgcctcca tcacatttgt gatctgtage tctggataca
                                                                       360
totoctgaca gtactgaaga acttottett ttgtttcaaa agcaactott ggtgcctgtt
                                                                       420
ngatcaggtt cccatttccc agtccgaatg ttcacatggc atatnttact tcccacaaaa
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      <211> 477
      <212> DNA
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      <220>
      <221> misc_feature
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                                                                       120
cccacgcagg cagcagcggg gccggtcaat gaactccact cgtggcttgg ggttgacggt 180
taantgoagg aagaggotga coacetogog gtocaceagg atgocogact gtgogggaco
tgcagcgaaa ctcctcgatg gtcatgagcg ggaagcgaat gangcccagg gccttgccca
gaacetteeg cetgttetet ggegteacet geagetgetg cegetnacae teggeetegg
accageggae aaaeggegtt gaacageege accteaegga tgeecantgt gtegegetee
aggaacggen ccagegtgtc caggtcaatg teggtgaane eteegegggt aatggeg
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     <211> 377
     <212> DNA
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<213> Homo sapien

<221> misc feature

<220>

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    agtocgagca geoccagace getgeegeec gaagetaage etgeetetgg cetteceete
                                                                                                                                            120
    cgcctcaatg cagaaccant agtgggagca ctgtgtttag agttaagagt gaacactgtn
                                                                                                                                            180
tgattttact tgggaatttc ctctgttata tagcttttcc caatgctaat ttccaaacaa
                                                                                                                                            240
  caacaacaaa ataacatgtt tgcctgttna gttgtataaa agtangtgat tctgtatnta
                                                                                                                                            300
    aagaaaatat tactgttaca tatactgctt gcaanttctg tatttattgg tnctctggaa
                                                                                                                                            360
    ataaatatat tattaaa
                                                                                                                                            377
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               <211> 495
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               \langle 223 \rangle n = A, T, C or G
               <400>_94 / Help Help ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( ) / ( )
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    cgagctgang cagatttccc acagtgaccc cagagccctg ggctatagtc tctgacccct
                                                                                                                                            120
    gaaggcccca ttccggggct gttccccgag gaggaaggga aggggctctg tgtgcccccc 240
    acqaqqaana qqcctqant cctqqqatca nacaccctt cacqtqtatc cccacacaaa 300
    tgcaagetca ccaaggtccc etetcaqtcc ettccetaca ccetgaacgg neactggccc
    acacccaccc agancancca cccgccatgg ggaatgtnct caaggaatcg cngggcaacg 420
    tqqactctnq tcccnnaaqq qqqcagaatc tccaatagan gganngaacc cttgctnana
    aaaaaaana aaaaa
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                                                                                                                                            120
tagetgtttt gagttgatte geaccactge accacacte aatatgaaaa etatttnact
                                                                                                                                            180
tatttattat cttgtgaaaa gtatacaatg aaaattttgt tcatactgta tttatcaagt
                                                                                                                                            240
atgatgaaaa gcaatagata tatattettt tattatgttn aattatgatt gccattatta
                                                                                                                                            300
   atoggcaaaa tgtggagtgt atgttctttt caeagtaata tatgcctttt gtaacttcac
                                                                                                                                            360
    ttggttattt tattgtaaat gaattacaaa attcttaatt taagaaaatg gtangttata
                                                                                                                                            420
   tttanttcan taatttcttt ccttgtttac gttaattttg aaaagaatgc at
                                                                                                                                            472
                                                                                                                        J. 12 3.
               <210> 96
               <211> 476
                                                                                                       ASSETTIONS FOR LOSS
               <212> DNA
               <213> Homo sapien
```

elizet seat s

```
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      <221> misc feature
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gtggtgaaat ttcaaaatta tatgtaactt ctactagttt tactttctcc cccaagtctt
                                                                          120
ttttaactca tgatttttac acacacaatc cagaacttat tatatagcct ctaagtcttt
                                                                          180
                                                                          240
attetteaca gtagatgatg aaagagteet ceagtgtett gngcanaatg ttetagntat
agctggatac atacngtggg agttctataa actcatacct cagtgggact naaccaaaat
                                                                          300
tgtgttagtc tcaattccta ccacactgag ggagcctccc aaatcactat attcttatct
                                                                          360
gcaggtactc ctccagaaaa acngacaggg caggcttgca tgaaaaagtn acatctgcgt
                                                                          420
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                                                                          476
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      <211> 479
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      <220>
      <221> misc feature
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      <223> n = A, T, C or G
                  Commence of the Commence of the Commence of
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aaataatgct gcaaacttaa tgttcttatg caaaatggaa cgctaatgaa acacagctta
caatcgcaaa tcaaaactca caagtgctca tctgttgtag atttagtgta ataagactta
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gattgtgctc cttcggatat gattgtttct canatcttgg gcaatnttcc ttagtcaaat
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caggetacta gaattetgtt attggatatn tgagageatg aaatttttaa naatacaett
                                                                          300
gtgattatna aattaatcac aaatttcact tatacctgct atcagcagct agaaaaacat
ntnnttttta natcaaagta ttttgtgttt ggaantgtnn aaatgaaatc tgaatgtggg
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                                                                          120
tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga agtgattcag tttcctctac ggatgagaga ctggctcaag aatatcctca tgcagcttta tgaagccact ctgaacacgc tggttatcta gatgagaaca gagaaataaa gtcagaaaat
                                                                          180
                                                                          240
                                                                          300
ttacctggag aaaagaggct ttggctgggg accatcccat tgaaccttct cttaaggact
                                                                          360
ttaagaaaaa ctaccacatg ttgtgtatcc tggtgccggc cgtttatgaa ctgaccaccc
                                                                          420
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                                                                           461
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      <212> DNA
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| cggtgagaaa aq                  | gccttctct         | agcgatctga                       | gaggcgtgcc                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | ttgggggtac                    | С                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 171        |
|--------------------------------|-------------------|----------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| . <210> 1                      | ·<br>100          | 1                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               | . *                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |            |
| <211> 2                        |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |            |
| <212> I                        |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |            |
|                                | Homo sapie        | en .                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |            |
| ••                             | , -               |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |            |
| <400> 1                        |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |            |
| cggccgcaag to                  |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 60         |
| cgactgcgac ga<br>aaggctgagc to |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 120<br>180 |
| cagccggaac ag                  |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 240        |
| cgagagatac go                  |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 3                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 269        |
|                                |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               | •                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |            |
| <210> 1                        | 3.                |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               | •                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |            |
| <211> 4                        |                   | ,                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | •                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |            |
| <212> I                        | JNA<br>Homo sapie | an                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |            |
| 12137 1                        | iomo bapro        | 1                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | . 2                           | •                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | ė          |
| <400> 1                        | - <u> </u>        |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 1                             | •                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | ŧ          |
| ttttttttt tt                   |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 60         |
| gctagcaagg ta                  |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 120        |
| ttgattggtt to                  |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 180<br>240 |
| tgaccgtcat tt                  |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 300        |
| ctgttctgga gg                  |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 360        |
| gatgatcagt ac                  |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 405        |
| \$                             | ring.<br>Sign     | in district in the               | international design of the second se | さが こうかまして<br>音 2 リブ (ウオー) よ   | n for a superior of the contract of the contra |            |
| <210> 1                        | L02               | r granda ya                      | 13 2 2 2 3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | a ji <u>t</u> ida a           | port of the first                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |            |
| <211> 4<br><212> 1             | 1 / U             | English San San San              | Total for the last                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                               | partial section of the second                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |            |
|                                | lomo sapie        | en                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | farthar a                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |            |
|                                |                   | 77                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Bir of the fit.<br>And Bergie | ing the state of t |            |
| <400> 1                        | .02               |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |            |
|                                |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 60         |
| ggcacttaat co                  |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 120<br>180 |
| atatacttct tt                  |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 240        |
| caaagtacaa tt                  |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 300        |
| ccgcaaaggt ta                  |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 360        |
| aaatcttagg gg                  |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               | ttgtttattt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 420        |
| tttaaacca tt                   | gtttgggc          | er production of the contract of |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               | •                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 470        |
| <210> 1                        | .03               |                                  | Mark of Mark                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |            |
| <211> 5                        | 81                |                                  | The first of the control of the cont | •                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |            |
| <212> D                        | NA                |                                  | in Park yang Salah kalendari<br>Salah kalendari Salah kalendari                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |            |
| <213> H                        | lomo sapie        | n .                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               | r ge                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |            |
| <400> 1                        | *                 | 13 13 to 12                      | pergar i ab                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |            |
| ttttttttt tt                   | .03               |                                  | ي ويلا مطرمت م                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | agttaccatt                    | ttattttact                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 60         |
| tacacatatt ta                  |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 120        |
| taaatggaaa ct                  | gccttaga          | tacataattc                       | ttaggaatta                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | gcttaaaatc                    | tgcctaaagt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 180        |
| gaaaatcttc tc                  | tagctctt          | ttgactgtaa                       | atttttgact                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | cttgtaaaac                    | atccaaattc                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 240        |
| atttttcttg to                  | tttaaaat          | tatctaatct                       | ttccatttt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | tecetattee                    | aagtcaattt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 300        |
| gcttctctag cc<br>agggaaaaca gg |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 360<br>420 |
| acgttaataa aa                  |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 480        |
|                                |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | aduct tade.                   | CCCCCCCCC                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |            |
| ccattttagt ca                  |                   |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 540        |

| tcaaaagcta | atataagata   | tttcacatac           | tcatctttct                            | g                                                                                                             |                                        |        | 581   |
|------------|--------------|----------------------|---------------------------------------|---------------------------------------------------------------------------------------------------------------|----------------------------------------|--------|-------|
| 1          |              |                      |                                       |                                                                                                               |                                        |        |       |
| •          | > 104        |                      |                                       |                                                                                                               |                                        |        | •     |
| <2112      |              |                      | *                                     |                                                                                                               |                                        |        |       |
|            | > DNA        | •                    |                                       |                                                                                                               |                                        |        |       |
| <2133      | > Homo sapie | en .                 |                                       |                                                                                                               |                                        | ,      |       |
| <400>      | . 104        |                      |                                       |                                                                                                               | •                                      |        |       |
|            |              | +++++-+-++           | a+++++++                              | gaaatgagga                                                                                                    | +                                      |        | 60    |
|            |              |                      |                                       | ctttaaaata                                                                                                    |                                        |        | 120   |
|            |              |                      |                                       | actggcttat                                                                                                    |                                        |        | 180   |
|            |              |                      |                                       | agtactacct                                                                                                    |                                        |        | 240   |
|            |              |                      |                                       | atttgtatca                                                                                                    |                                        |        | 300   |
|            |              |                      |                                       |                                                                                                               | tatagcatta                             |        | 360   |
|            |              |                      |                                       | tagttggcag                                                                                                    |                                        |        | 420   |
|            |              |                      |                                       | gttaaatatc                                                                                                    |                                        | •      | 480   |
|            |              |                      |                                       | tttacaagca                                                                                                    |                                        |        | 540   |
|            |              | cctagcccaa           |                                       |                                                                                                               |                                        |        | 578   |
|            |              |                      |                                       |                                                                                                               |                                        |        |       |
| <210>      |              |                      |                                       |                                                                                                               |                                        |        |       |
| <211>      | > 538        |                      |                                       |                                                                                                               |                                        |        | ٠.    |
| <212>      | > DNA        |                      | * .                                   |                                                                                                               |                                        |        | . :   |
| <213>      | Homo sapie   | en                   |                                       |                                                                                                               |                                        |        | ;     |
| *.         |              | e jay ya e e e       | 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 | Burney Bridge                                                                                                 | :                                      |        |       |
| <400>      |              | • •                  |                                       | $(\mathcal{A}_{i}) = \mathcal{A}_{i} \otimes \mathcal{A}_{i} \otimes \mathcal{A}_{i} \otimes \mathcal{A}_{i}$ |                                        |        | : •   |
|            |              |                      |                                       | ttttatattt                                                                                                    |                                        |        | 60    |
|            |              |                      |                                       | tgatcagagg                                                                                                    |                                        |        | 120   |
|            |              |                      |                                       |                                                                                                               | taaattattt                             | • •    | 180   |
|            |              |                      |                                       | tcagaaactc                                                                                                    |                                        | .,     | 240   |
|            |              |                      |                                       |                                                                                                               | tgatgaatat                             | .*     | 300   |
|            |              |                      |                                       | tacttagtga                                                                                                    |                                        |        | 360   |
|            |              |                      |                                       | ctttcttcaa                                                                                                    |                                        |        | 420   |
|            |              |                      |                                       | gttctttcta                                                                                                    |                                        |        | 480   |
| agatatgttt | cctttgccaa   | tattaaaaaa           | ataataatgt                            | ttactactag                                                                                                    | tgaaaccc                               | • .    | 538   |
| <210>      | 106          |                      |                                       |                                                                                                               | -                                      |        |       |
| <211>      |              | •                    |                                       |                                                                                                               | •                                      |        |       |
| <212>      |              |                      | •                                     |                                                                                                               |                                        | . :    |       |
|            | Homo sapie   | en ·                 | •                                     |                                                                                                               |                                        |        |       |
|            |              |                      |                                       | · ·                                                                                                           |                                        |        |       |
| <400>      | 106          |                      |                                       |                                                                                                               |                                        |        |       |
| tttttttt   | ttttttagtc   | aagtttctat           | ttttattata                            | attaaagtct                                                                                                    | tggtcatttc                             | · -, f | :60   |
| atttattagc | tctgcaactt   | acatatttaa           | attaaagaaa                            | cgttttagac                                                                                                    | aactgtacaa                             |        | 120   |
| tttataaatg | taaggtgcca   | ttattgagta           | atatattcct.                           | ccaagagtgg                                                                                                    | atgtgtccct.                            |        | 180   |
|            |              |                      |                                       | attagtagat                                                                                                    |                                        |        | 240   |
|            |              |                      |                                       |                                                                                                               | gagttggtag                             |        |       |
|            |              |                      |                                       |                                                                                                               | cggtgaaaat                             |        | 360   |
|            |              |                      |                                       |                                                                                                               | actcttcgaa                             |        | 420   |
| ccgcttcctc | aaaggcgctg   | ccacatttgt           | ggctctttgc                            | acttgtttca                                                                                                    |                                        |        | 473   |
|            |              | Market William       | A 2 2 3 2 2 3                         | 1                                                                                                             |                                        |        |       |
| <210>      |              | •                    |                                       |                                                                                                               | _                                      | ¥* '   |       |
|            | 1621         | <i>;</i> ·           |                                       |                                                                                                               |                                        |        | • : : |
| <212>      |              |                      |                                       | 1.5                                                                                                           |                                        |        |       |
| <213>      | · Homo sapie | <b>≥n</b> lea de lea | A                                     | Fig. 7 - Your York                                                                                            |                                        | ;      | ٠.,   |
| 2100-      | 107          |                      |                                       |                                                                                                               | ** .                                   |        |       |
| <400>      | •            | 1.1<br>+             |                                       |                                                                                                               | اد اداد داد اداد اداد اداد اداد اداد ا |        |       |
| cyccatggca | ctycagggca   | ccccggccat           | yyayetgtee                            | ggcctggccc                                                                                                    | egggeeegtt                             |        | 60    |
| ccycgctatg | gradigatg    | acticggggc           | gegegegea                             | cgcgtggacc                                                                                                    | ggcccggctc                             |        | 120   |

|                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | •                                                                                 |                                                                                                                                                                                                                                  |
|-----------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ccgctacgac gtgagccgct | tgggccgggg caag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | cgctcg ctagtgctgg                                                                 | acctgaagca 180                                                                                                                                                                                                                   |
| gccgcgggga gccgccgtgc |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                   |                                                                                                                                                                                                                                  |
| cttccgccgc ggtgtcatgg | agaaactcca gctg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | ggccca gagattctgc                                                                 | agcgggaaaa 300                                                                                                                                                                                                                   |
| tccaaggctt atttatgcca | ggctgagtgg attt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | ggccag tcaggaagct                                                                 | tetgeeggtt 360                                                                                                                                                                                                                   |
| agctggccac gatatcaact | atttggcttt gtca                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | ggtgtt ctctcaaaa                                                                  | ttggcagaag 420                                                                                                                                                                                                                   |
| tggtgagaat ccgtatgccc | cgctgaatct cctg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | gctgac tttgctggtg                                                                 | gtggcettat 480                                                                                                                                                                                                                   |
| gtgtgcactg ggcattataa | tggctctttt tgac                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | cgcaca cgcactgaca                                                                 | agggtcaggt 540                                                                                                                                                                                                                   |
| cattgatgca aatatggtgg | aaggaacagc atat                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | ttaagt tottttotgt                                                                 | ggaaaactca 600                                                                                                                                                                                                                   |
| gaaatcgagt ctgtgggaag | cacctcgagg acag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | aacatg ttggatggtg                                                                 | gagcaccttt 660                                                                                                                                                                                                                   |
| ctatacgact tacaggacag | cagatgggga atte                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | atgget gttggageaa                                                                 | tagaacccca 720                                                                                                                                                                                                                   |
| gttctacgag ctgctgatca | aaggacttgg acta                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | aagtet gatgaactte                                                                 | ccaatcagat 780                                                                                                                                                                                                                   |
| gagcatggat gattggccag |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                   |                                                                                                                                                                                                                                  |
| gaaggcagag tggtgtcaaa |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                   |                                                                                                                                                                                                                                  |
| ttttgaggag gttgttcatc |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                   |                                                                                                                                                                                                                                  |
| ggagcaggac gtgagccccc |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                   |                                                                                                                                                                                                                                  |
| tttcaaaagg gatcctttca |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                   |                                                                                                                                                                                                                                  |
| cageegegaa gagatttate | agcttaactc agat                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | aaaato attgaaagta                                                                 | ataaggtaaa 1140                                                                                                                                                                                                                  |
| agctagtctc taacttccag | gcccacggct caag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | tgaatt tgaatactgo                                                                 | atttacagtg 1200                                                                                                                                                                                                                  |
| tagagtaaca cataacattg |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                   |                                                                                                                                                                                                                                  |
| ccactctaat caagaaaaga | attacagact ctga                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | ttctac agtgatgatt                                                                 | gaattctaaa 1320                                                                                                                                                                                                                  |
| aatggttatc attagggctt | ttgatttata aaac                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | tttggg tacttatact                                                                 | aaattatggt 1380                                                                                                                                                                                                                  |
| agttattctg ccttccagtt |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                   |                                                                                                                                                                                                                                  |
| ttttgaatgg gttctagtga |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | <del>-</del>                                                                      |                                                                                                                                                                                                                                  |
| atttacactc ttgattctac |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                   |                                                                                                                                                                                                                                  |
| aaaagtcacg tgaaacaaaa |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                   |                                                                                                                                                                                                                                  |
|                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                   | 1621                                                                                                                                                                                                                             |
| V 1010                | and the second s | ប្រាស់ ក្រុមប្រជាជន្លាំ ។ បានប្រាស់<br>បានសាល់ស្នាស់ស្នាស់ស្នាស់ សាស់សាល់សាល់សាល់ |                                                                                                                                                                                                                                  |
|                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | ತ (* ) ಸಹಕ್ಕೆ ಅಭಿವರ್ಣದು<br>(ಇಂದಾ ಹತ್ತು ಪಡೆದ ಕರ್ಮಾಗ ()                             |                                                                                                                                                                                                                                  |
| <211> 382             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                   |                                                                                                                                                                                                                                  |
| <212> PRT             | مائية أو الله الله الله الله الله الله الله الل                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | enako arabenako bi.<br>Morengana nako baren                                       | en e                                                                                                                                                                                         |
| <213> Homo sapi       | en :                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                   | e deel e die gebruik van die g<br>Die gebruik van die gebruik va |
| <400> 108             | and a set of the set o |                                                                                   | andre de la companya de la companya<br>La companya de la co |
| Met Ala Leu Gln Gly I |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                   |                                                                                                                                                                                                                                  |
| 1 5                   | le ser var met G                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                   | 15                                                                                                                                                                                                                               |
| Gly Pro Phe Cys Ala M | et Val Leu Ala A                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | sp Phe Gly Ala Ar                                                                 | g Val Val                                                                                                                                                                                                                        |

30 **25** · 20 Arg Val Asp Arg Pro Gly Ser Arg Tyr Asp Val Ser Arg Leu Gly Arg 45 40 Gly Lys Arg Ser Leu Val Leu Asp Leu Lys Gln Pro Arg Gly Ala Ala 60 55 Arg Arg Gly Val Met Glu Lys Leu Gln Leu Gly Pro Glu Ile Leu Gln ქენა - ელემადა. 85) მე რინანა ქესიტ00 → მამა თუკუ - 195 - ესის თ Arg Glu Asn Pro Arg Leu Ile Tyr Ala Arg Leu Ser Gly Phe Gly Gln 🔻 🗀 🗀 <sub>ເຂ</sub>ົ້າໃນ ທີ່ສະເ**ນີ 00** ຊຸລູສັ້ນ ພາຍຊຸດສູນໃຊ້ ທີ່**105**,ສຣາກິດ ຄວາມກູສະດາຊິ**ດ 110**ສາຣະ ຄົນ ພາກ ການ ການ Ser Gly Ser Phe Cys Arg Lew Ala Gly His Asp Ile Asn Tyr Lew Ala ញ់ ប្រាសាធិស្សា ស្រីស្សាស្រី **រៀបប្រាសិក្**រាស់ ស្រាប់ រៀបប្រាសិក្សាស្រី ស្រាប់ **រៀបប្រាសាធិស្សា** ស្រាស់ ស្រាប់ ស្រាប់ Leu Ser Gly Val Leu Ser Lys Ile Gly Arg Ser Gly Glu Asn Pro Tyr 140 135 12. Ala Pro Leu Asn Leu Leu Ala Asp Phe Ala Gly Gly Leu Met Cys 💛 155 160 150 Ala Leu Gly Ile Ile Met Ala Leu Phe Asp Arg Thr Arg. Thr Asp Lys (180) 165 175 170 Gly Gln Val Ile Asp Ala Asn Met Val Glu Gly Thr Ala Tyr Leu Ser Com 180 (A. 15) (6) (6) (9) (3**185**(5) (819 (1.5) (1.5) (1.5) (1.6) (1.90 (1.5) (1.5) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) (1.6) ( Ser Phe Leu Trp Lys Thr Gln Lys Ser Ser Leu Trp Glu Ala Pro Arg

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200
                                              205
       195
Gly Gln Asn Met Leu Asp Gly Gly Ala Pro Phe Tyr Thr Thr Tyr Arg
                      , 215
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Thr Ala Asp Gly Glu Phe Met Ala Val Gly Ala Ile Glu Pro Gln Phe
                   230
                                      235
Tyr Glu Leu Leu Ile Lys Gly Leu Gly Leu Lys Ser Asp Glu Leu Pro
              - 245
                                  250
Asn Gln Met Ser Met Asp Asp Trp Pro Glu Met Lys Lys Phe Ala
                              265
                                                  270
Asp Val Phe Ala Lys Lys Thr Lys Ala Glu Trp Cys Gln Ile Phe Asp
                           280
                                            285
Gly Thr Asp Ala Cys Val Thr Pro Val Leu Thr Phe Glu Glu Val Val
                      295
                                          300
His His Asp His Asn Lys Glu Arg Gly Ser Phe Ile Thr Ser Glu Glu
               310
                                    315
Gln Asp Val Ser Pro Arg Pro Ala Pro Leu Leu Asn Thr Pro Ala
               325
                        . 1
                                  330
Ile Pro Ser Phe Lys Arg Asp Pro Phe Ile Gly Glu His Thr Glu Glu
                              345
                                                  350
           340
Ile Leu Glu Glu Phe Gly Phe Ser Arg Glu Glu Ile Tyr Gln Leu Asn
                         360
                                              365
Ser Asp Lys Ile Ile Glu Ser Asn Lys Val Lys Ala Ser Leu
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   370
                       375 🐇
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      <212> DNA
     <213> Homo sapien
     <400> 109
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<211> 3410 <212> DNA <213> Homo sapien

<400> 110

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| gaggtcttat ctctcagggg                                                                                                                                                                                                                                                                                                                                                                                                           | agatttaaat a                                                                                                                                                            | recatttaca                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | ataatotcot                                                                                                                                         | cttatttatt                                                                                          | 3240                         |
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| aaattaaagg ctttcttata                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                    | aaaaaaaaa                                                                                           | 3360                         |
| ' aaaaaaaara aaaaaaaaaa                                                                                                                                                                                                                                                                                                                                                                                                         | aaaaaaaaa a                                                                                                                                                             | aaaaaataa                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | aaaaaaaaa                                                                                                                                          |                                                                                                     | 3410                         |
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| <210> 111                                                                                                                                                                                                                                                                                                                                                                                                                       | 4                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                    |                                                                                                     |                              |
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| <211> 1289                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                    |                                                                                                     |                              |
| <212> DNA                                                                                                                                                                                                                                                                                                                                                                                                                       | •                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | •                                                                                                                                                  |                                                                                                     | •                            |
| <213> Homo sapi                                                                                                                                                                                                                                                                                                                                                                                                                 | en                                                                                                                                                                      | .*                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                    |                                                                                                     |                              |
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| <400> 111                                                                                                                                                                                                                                                                                                                                                                                                                       | •                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                    |                                                                                                     |                              |
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| gtggagcctc agcagttccc                                                                                                                                                                                                                                                                                                                                                                                                           | tetttcagaa c                                                                                                                                                            | ctcactgcca                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | agagccctga                                                                                                                                         | acaggagcca                                                                                          | 120                          |
| ccatgcagtg cttcagcttc                                                                                                                                                                                                                                                                                                                                                                                                           | attaagacca t                                                                                                                                                            | gatgatect                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | cttcaatttg                                                                                                                                         | ctcatctttc                                                                                          | 180                          |
| tgtgtggtgc agccctgttg                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                    |                                                                                                     | 240                          |
| tgaagatett cgggccactg                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                    |                                                                                                     | 300                          |
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| tcatcgcagc cggcgttgtg                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                    |                                                                                                     | 360                          |
| ctgagagcaa gtgtgccctc                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                    |                                                                                                     | 420                          |
| aggttgcagc tgctgtggtc                                                                                                                                                                                                                                                                                                                                                                                                           | gccttggtgt a                                                                                                                                                            | caccacaat                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | ggctgagcac                                                                                                                                         | ttcctgacgt                                                                                          | 480                          |
| tgctggtagt gcctgccatc                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                    |                                                                                                     | 540                          |
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| actcacccta cttcaaagag                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                    |                                                                                                     | 660                          |
| ccaacacagc caatgaaacc                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                    |                                                                                                     | 720                          |
| gcttcaatca gcttttgtat                                                                                                                                                                                                                                                                                                                                                                                                           | gacatccgaa c                                                                                                                                                            | ctaatgcagt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | caccgtgggt                                                                                                                                         | ggtgtggcag                                                                                          | 780                          |
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|                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                    |                                                                                                     | ` 960                        |
| accetggeaa geageagtga                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                    |                                                                                                     |                              |
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|                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | ggoaccoag                                                                                                                                          | agcucutaag                                                                                          |                              |
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                                                     280 g - 1 g - 285 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 g - 1 
 Trp Val Ala Glu Ala Leu Ser Arg Ser Ala Leu Leu Pro Pro Gly Gly and the
                                                 Pro Pro Pro Pro Asp Leu Pro Gly Ser Lys Asp
                   310 (210 × 113 (211 × 553 ) (212 × 573 ) (212 × 573 ) (213 × 573 ) (213 × 573 ) (213 × 573 ) (213 × 573 ) (213 × 573 ) (213 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 573 × 
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                 <210> 113
                 <211> 553
<212> PRT
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                  ्रा । प्राप्त प्रकृति । इक्षुत्र विकासकारिक क्षेत्र । विकास विकास करणा प्राप्त प्राप्त । विकास विकास
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                                                Gln Leu Leu Val Asn Leu Leu Thr Phe Gly Leu Glu Val Cys Leu
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Ala Ala Gly Ile Thr Tyr 'Val Pro Pro Leu Leu Glu Val Gly Val
                                                                                    40
Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly ...
Leu Val Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly
Arg Tyr Gly Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile
                                     ., 485 c. g. g. e. j. g. 90 c. e. j. g., 95 e. ar
Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu
                                   100 100 110 110 1
Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly
                       Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu
           130
Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala
145
Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr
                              175 cm. 165
Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu
                                   Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu
195
Thr Cys Val Ala Ala Thr Leu Leu Val Ala Glu Glu Ala Ala Leu Gly
210 215 220 Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His
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230 235 Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu 245 250 Leu Pro Arg Leu His Gln Leu Cys Cys Arg Met Pro Arg Thr Leu Arg 265 Arg Leu Phe Val Ala Glu Leu Cys Ser Trp Met Ala Leu Met Thr Phe 280 285 Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu Gly Leu Tyr Gln Gly Val 290 295 300 Pro Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly 310 315 Val Arg Met Gly Ser Leu Gly Leu Phe Leu Gln Cys Ala Ile Ser Leu 325 330 335 Val Phe Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg 340 345 Ala Val Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala 355 360 365 Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu 375 380 Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala 390 395 Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro Lys Tyr Arg Gly 410 405 Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser Leu Met Thr Ser Phe Leu 420 425 430 Pro Gly Pro Lys Pro Gly Ala Pro Phe Pro Asn Gly His Val Gly Ala 440 Gly Gly Ser Gly Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser 455 460 Ala Cys Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala 470 475 Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp 485 490 495 Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met Gly Ser 505 510 500 Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met Val Ser Ala Ala 520 525 Gly Leu Gly Leu Val Ala Ile Tyr Phe Ala Thr Gln Val Val Phe Asp 535 540 Lys Ser Asp Leu Ala Lys Tyr Ser Ala 550

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 Lys
 Thr
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 Asn
 Leu

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 Ile
 Phe
 Leu
 Cys
 Gly
 Ile
 Ile
 Trp
 Val
 Val
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| C1                     |                                                                       |                                                                                     |                                                                  |                                       |                                           |                              |                          |                              |                          |                            |                      |                      |                       |                         |                   |
|------------------------|-----------------------------------------------------------------------|-------------------------------------------------------------------------------------|------------------------------------------------------------------|---------------------------------------|-------------------------------------------|------------------------------|--------------------------|------------------------------|--------------------------|----------------------------|----------------------|----------------------|-----------------------|-------------------------|-------------------|
| GIU                    | Ser Ly                                                                | в Суз                                                                               | Ala<br>85                                                        | Leu                                   | Val                                       | Thr                          | Phe                      | Phe<br>90                    | Phe                      | Ile                        | Leu                  | Leu                  | Leu<br>95             | Ile                     |                   |
| • Phe                  | Ile Ala                                                               |                                                                                     | Val                                                              | Ala                                   | Ala                                       | Ala                          |                          | Val                          |                          |                            | Val                  | -                    | Thr                   | Thr                     |                   |
| Met                    | Ala Glu                                                               |                                                                                     |                                                                  | Leu                                   | Thr                                       |                              | Leu                      | Val                          |                          | Pro                        |                      |                      |                       | Lys                     |                   |
| _                      | 11:<br>Tyr Gly                                                        |                                                                                     | Ğln                                                              | Glu                                   |                                           | Phe                          | Thr                      | Gln                          | Val-                     |                            | Asn                  | Thr                  |                       | Met                     |                   |
|                        | 130<br>Gly Leı                                                        | ı Lys                                                                               | Cys                                                              | Суз                                   | 135<br>Gly                                | Phe                          | Thr                      | Asn                          | Tyr                      | 140<br>Thr                 | Asp                  | Phe                  | Glu                   | Asp                     | •                 |
| 145<br>Ser             | Pro Ty                                                                | Phe                                                                                 | Lvs                                                              | 150<br>Glu                            |                                           | Ser                          |                          |                              |                          |                            |                      |                      |                       | 160<br>Asp              |                   |
|                        | Asn Val                                                               |                                                                                     | 165                                                              |                                       |                                           |                              |                          | 170                          | , F ·                    | 1                          | s. 3                 | ; :,                 | 175                   | 14. J. 14.              |                   |
|                        |                                                                       | 180                                                                                 |                                                                  |                                       |                                           |                              | 185                      |                              |                          |                            |                      | 190                  | , d =                 |                         | :                 |
| His .                  | Asp Glr<br>195                                                        |                                                                                     |                                                                  |                                       |                                           |                              |                          |                              |                          |                            |                      |                      |                       | Ile                     |                   |
|                        | Thr Asr<br>210                                                        |                                                                                     | Val                                                              | Thr                                   |                                           |                              |                          |                              |                          |                            |                      |                      |                       | Gly                     |                   |
|                        | Glu Let                                                               | Ala                                                                                 |                                                                  |                                       | Ile                                       | Val                          | Ser                      | Met                          | Tyr                      | Leu                        | Tyr                  | Суѕ                  | Asn                   |                         |                   |
| Gln                    |                                                                       |                                                                                     | •                                                                | 250                                   |                                           |                              | · ·                      | . :                          | 233                      |                            | ** .                 |                      |                       | 240                     |                   |
|                        |                                                                       |                                                                                     |                                                                  | •                                     | • • •                                     |                              |                          |                              | . ,                      |                            | •                    | •                    |                       | ٠,                      | •                 |
|                        | <210>                                                                 |                                                                                     |                                                                  |                                       |                                           |                              | -                        |                              |                          | ,`                         |                      |                      | ,                     |                         |                   |
|                        | <211>                                                                 |                                                                                     |                                                                  |                                       |                                           |                              |                          |                              |                          |                            |                      |                      |                       | 5-2                     |                   |
|                        | <212>                                                                 | •                                                                                   |                                                                  |                                       |                                           | · ·                          |                          |                              | *                        | •                          | •                    | • "                  |                       |                         | •                 |
|                        | <2132                                                                 | Home                                                                                | o sar                                                            | pien                                  | •                                         |                              |                          |                              | *:                       | .:                         |                      |                      |                       |                         |                   |
|                        | <400>                                                                 | 115                                                                                 |                                                                  | •                                     |                                           |                              | -                        |                              | . (                      |                            | i d<br>Figs          | 1                    | • •                   | n film                  |                   |
|                        | tttctc                                                                |                                                                                     |                                                                  |                                       |                                           |                              |                          |                              |                          |                            |                      |                      |                       |                         | v:60              |
|                        | tcactg                                                                |                                                                                     |                                                                  |                                       |                                           |                              |                          |                              |                          |                            |                      |                      |                       |                         | 120               |
|                        | tttgtg                                                                |                                                                                     |                                                                  |                                       |                                           |                              |                          |                              |                          |                            |                      |                      |                       |                         |                   |
|                        | gtagaa<br>agaacc                                                      |                                                                                     |                                                                  |                                       |                                           |                              |                          |                              |                          |                            |                      |                      |                       |                         | 240<br>300        |
|                        | tacatg                                                                |                                                                                     |                                                                  |                                       |                                           |                              |                          |                              |                          |                            |                      |                      |                       |                         | 360               |
| ttag                   |                                                                       |                                                                                     |                                                                  |                                       |                                           |                              |                          | _                            | i ·                      |                            | :                    |                      |                       |                         | 366               |
|                        |                                                                       |                                                                                     |                                                                  |                                       |                                           |                              |                          |                              |                          | ٠.                         |                      |                      |                       |                         |                   |
|                        | <210>                                                                 |                                                                                     |                                                                  | •                                     |                                           |                              |                          |                              |                          | · · · · · (                | •                    | -                    |                       |                         | •                 |
|                        | <211>                                                                 |                                                                                     |                                                                  |                                       |                                           |                              |                          |                              |                          |                            |                      |                      |                       |                         |                   |
|                        |                                                                       |                                                                                     |                                                                  |                                       |                                           |                              |                          |                              |                          |                            |                      |                      | •                     |                         |                   |
|                        |                                                                       | DNA<br>Home                                                                         | , ear                                                            | i an                                  |                                           |                              |                          |                              |                          |                            |                      |                      |                       |                         |                   |
|                        | <213>                                                                 |                                                                                     | sap                                                              | oien                                  |                                           |                              |                          |                              | •                        |                            | •                    |                      |                       |                         |                   |
|                        |                                                                       | Homo                                                                                | sar                                                              | oien                                  |                                           |                              |                          |                              | •                        | •                          |                      |                      |                       |                         |                   |
|                        | <213><br><220><br><221>                                               | Homo                                                                                | _fea                                                             | ıture                                 | <b>.</b>                                  |                              |                          |                              | :                        |                            |                      |                      |                       |                         |                   |
|                        | <213><br><220><br><221><br><222>                                      | Homo miso (1).                                                                      | _fea                                                             | iture<br>282)                         |                                           |                              |                          |                              | •                        |                            |                      |                      |                       |                         |                   |
|                        | <213><br><220><br><221>                                               | Homo miso (1).                                                                      | _fea                                                             | iture<br>282)                         |                                           |                              |                          |                              |                          |                            |                      |                      |                       |                         |                   |
|                        | <213><br><220><br><221><br><222>                                      | misc<br>(1).                                                                        | _fea                                                             | iture<br>282)                         |                                           |                              |                          |                              |                          |                            |                      |                      |                       |                         |                   |
| acaa                   | <213> <220> <221> <221> <222> <223>                                   | misc (1).                                                                           | _fea<br>(2<br>A,T,                                               | ture<br>182)<br>C or                  | Ģ                                         | tage                         | <b>∵</b> aaa             | atta                         | aaa                      | tota                       | cccg                 | rta i                | teta                  | ıatatt                  | 60                |
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                                                                        120
aataaqqcaa aatatatqaa acaacaqqtc tcqaqatatt ggaaatcaqt caatgaagga
                                                                        180
                                                                        240
tactgatccc tgatcactgt cctaatgcag gatgtgggaa acagatgagg tcacctctgt
gactgcccca gcttactgcc tgtagagagt ttctangctg cagttcagac agggagaaat
                                                                        300
                                                                        305
tgggt
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                                                                         60
aantcctggg t
                                                                         71
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gaaaatgggg tgaaattggc caactttcta tnaacttatg ttggcaantt tgccaccaac
agtaagctgg cccttctaat aaaagaaaat tgaaaggttt ctcactaanc ggaattaant
                                                                        180
aatggantca aganactece aggeeteage gt
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                                                                         90
ctccgccggc gcagaacatg ctggggtggt
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                                                                        120
```

| •                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                  |                                                                              |                                                                               |                                                            |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|------------------------------------------------------------------------------|-------------------------------------------------------------------------------|------------------------------------------------------------|
| ctacagtctg catttggcag aaatgaagat                                                                                                                                                                                                                                                                                                                                                                                                                                         | gaatttggat                                                                       | taaatgagga                                                                   | toctoaacat                                                                    | 180                                                        |
| ttgcctcacc aaacaaagt gaaacaactg                                                                                                                                                                                                                                                                                                                                                                                                                                          | 20000330                                                                         | **********                                                                   | 22222222                                                                      | 240                                                        |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                  |                                                                              |                                                                               |                                                            |
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| ctctttgctt gt                                                                                                                                                                                                                                                                                                                                                                                                                                                            | •                                                                                | •                                                                            |                                                                               | 432                                                        |
| cccccgcc gc                                                                                                                                                                                                                                                                                                                                                                                                                                                              | •                                                                                | •                                                                            |                                                                               |                                                            |
| .010- 106                                                                                                                                                                                                                                                                                                                                                                                                                                                                | * *                                                                              |                                                                              |                                                                               |                                                            |
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| <213> Homo sapien                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 5 a                                                                              | *                                                                            |                                                                               | •                                                          |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                  | 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1                                        | 1.1                                                                           |                                                            |
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|                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                  |                                                                              |                                                                               |                                                            |
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|                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                  | •                                                                            |                                                                               | -                                                          |
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| ZETON HOMO BENEGI                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                  |                                                                              |                                                                               |                                                            |
| .400. 400                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                  | •                                                                            |                                                                               |                                                            |
| <400> 127                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                  |                                                                              |                                                                               |                                                            |
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| <213> Homo sapien                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                  |                                                                              |                                                                               |                                                            |
| <213> Holdo Sapten                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                  |                                                                              |                                                                               |                                                            |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                  |                                                                              |                                                                               |                                                            |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                  |                                                                              |                                                                               |                                                            |
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| acctcattag taattgtttt gttgtttcat acctgagata acagaatgaa aatggaagga ttetetetga agtetaggtt acceattttg ccaaagcatt tggacagttt cttgttgtgt tteetgeaaa aggeteacte agteeettge aggetgeett ettteeatg tee  <210> 129 <211> 192 <211> 192 <212> DNA <213> Homo sapien  <220> <221> misc_feature <222> (1)(192) <223> n = A,T,C or G  <400> 129 acatacatgt gtgtatattt ttaaatatea tgaaaacaca ctaacataat ttntgtgaac tagcacattc atctgtgata naaagatagg gataaacaaa gt                       | cagccagatt<br>gggacccatt<br>tttagaatgg<br>ttgctcagtg<br>cttttgtatc<br>catgatcaga | teteetttge ataggeaata tttteetttt gactgggete actetgactt tacaacceaa ttcettcacg | tctctgctca aacacagttc tcttagcctt cccagggcct  tttagcatac atcattcatc            | 120<br>180<br>240<br>300<br>323<br>60<br>120<br>180<br>192 |
| acctcattag taattgtttt gttgtttcat acctgagata acagaatgaa aatggaagga ttctctctga agtctaggtt acccattttg ccaaagcatt tggacagttt cttgttgtgt ttcctgcaaa aggctcactc agtcccttgc aggctgcctt ctttccatg tcc  <210> 129 <211> 192 <211> 192 <212> DNA <213> Homo sapien  <220> <221> misc_feature <222> (1)(192) <223> n = A,T,C or G  <400> 129 acatacatgt gtgtatattt ttaaatatca tgaaaacaca ctaacataat ttntgtgaac tagcacattc atctgtgata naaagatagg gataaacaaa gt  <210> 130            | cagccagatt<br>gggacccatt<br>tttagaatgg<br>ttgctcagtg<br>cttttgtatc<br>catgatcaga | teteetttge ataggeaata tttteetttt gactgggete actetgactt tacaacceaa ttcettcacg | tctctgctca aacacagttc tcttagcctt cccagggcct  tttagcatac atcattcatc ttggccaatg | 120<br>180<br>240<br>300<br>323<br>60<br>120<br>180<br>192 |
| acctcattag taattgtttt gttgtttcat acctgagata acagaatgaa aatggaagga ttetetetga agtetaggtt acceattttg ccaaagcatt tggacagttt cttgttgtgt tteetgeaaa aggeteacte agteeettge aggetgeett ettteeatg tee  <210> 129 <211> 192 <211> 192 <212> DNA <213> Homo sapien  <220> <221> misc_feature <222> (1)(192) <223> n = A,T,C or G  <400> 129 acatacatgt gtgtatattt ttaaatatea tgaaaacaca ctaacataat ttntgtgaac tagcacattc atctgtgata naaagatagg gataaacaaa gt                       | cagccagatt<br>gggacccatt<br>tttagaatgg<br>ttgctcagtg<br>cttttgtatc<br>catgatcaga | teteetttge ataggeaata tttteetttt gactgggete actetgactt tacaacceaa ttcettcacg | tctctgctca aacacagttc tcttagcctt cccagggcct  tttagcatac atcattcatc ttggccaatg | 120<br>180<br>240<br>300<br>323<br>60<br>120<br>180<br>192 |
| acctcattag taattgtttt gttgtttcat acctgagata acagaatgaa aatggaagga ttctctctga agtctaggtt acccattttg ccaaagcatt tggacagttt cttgttgtgt ttcctgcaaa aggctcactc agtcccttgc aggctgcctt ctttccatg tcc  <210> 129 <211> 192 <211> 192 <212> DNA <213> Homo sapien  <220> <221> misc feature <222> (1)(192) <223> n = A,T,C or G  <400> 129 acatacatgt gtgtatattt ttaaatatca tgaaaacaca ctaacataat ttntgtgaac tagcacattc atctgtgata naaagatagg gataaacaaa gt  <210> 130            | cagccagatt<br>gggacccatt<br>tttagaatgg<br>ttgctcagtg<br>cttttgtatc<br>catgatcaga | teteetttge ataggeaata tttteetttt gactgggete actetgactt tacaacceaa tteettcacg | tctctgctca aacacagttc tcttagcctt cccagggcct  tttagcatac atcattcatc ttggccaatg | 120<br>180<br>240<br>300<br>323<br>60<br>120<br>180<br>192 |
| acctcattag taattgtttt gttgtttcat acctgagata acagaatgaa aatggaagga ttctctctga agtctaggtt acccattttg ccaaagcatt tggacagttt cttgttgtgt ttcctgcaaa aggctcactc agtcccttgc aggctgcctt cttttccatg tcc  <210> 129 <211> 192 <211> 192 <212> DNA <213> Homo sapien  <220> <221> misc_feature <222> (1)(192) <223> n = A,T,C or G  <400> 129 acatacatgt gtgtatattt ttaaatatca tgaaaacaca ctaacataat ttntgtgaac tagcacattc atctgtgata naaagatagg gataaacaaa gt  <210> 130 <211> 362 | cagccagatt<br>gggacccatt<br>tttagaatgg<br>ttgctcagtg<br>cttttgtatc<br>catgatcaga | teteetttge ataggeaata tttteetttt gactgggete actetgactt tacaacceaa tteettcacg | tctctgctca aacacagttc tcttagcctt cccagggcct  tttagcatac atcattcatc ttggccaatg | 120<br>180<br>240<br>300<br>323<br>60<br>120<br>180<br>192 |

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      \langle 223 \rangle n = A,T,C or G
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tataatgacg caacaaaaag gtgctgttta gtcctatggt tcagtttatg cccctgacaa
                                                                  120
gtttccattg tgttttgccg atcttctggc taatcgtggt atcctccatg ttattagtaa
                                                                  180
ttctgtattc cattttgtta acgcctggta gatgtaacct gctangaggc taactttata
                                                                  240
 cttatttaaa agctcttatt ttgtggtcat taaaatggca atttatgtgc agcactttat
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tgcagcagga agcacgtgtg ggttggttgt aaagctcttt gctaatctta aaaagtaatg
                                                                  360
                                                                  362
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      <212> DNA
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                                                                 120
gttctcccag gttcgccctg ctgctccaag tctcagcagc agcctctttt aggaggcatc
                                                                 180
ttctgaacta gattaaggca gcttgtaaat ctgatgtgat ttggtttatt atccaactaa
                                                                 240
cttccatctg ttatcactgg agaaagccca gactccccan gacnggtacg gattgtgggc
                                                                 300
atanaaggat tgggtgaagc tggcgttgtg gt
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<211> 322
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                                                                 120
ctcaaattcc caaacagggg ctctgtggga aaaatgaggg aggacctttg tatctcgggt tttagcaagt taaaatgaan atgacaggaa aggcttattt atcaacaaag agaagagttg
                                                                 180
                                                                 240
ggatgcttct aaaaaaaact ttggtagaga aaataggaat gctnaatcct agggaagcct
                                                                . 300
gtaacaatct acaattggtc ca

<210> 133

<211> 278
     <212> DNA
     <213> Homo sapien
                                                       . A. 4.1 ETT.
     <220>
                                                          3.82
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                                                                     120
ctatttaaaa aaaatcacaa atctttccct ttaagctatg ttnaattcaa actattcctg
                                                                     180
ctattcctgt tttgtcaaag aaattatatt tttcaaaata tgtntatttg tttgatgggt
                                                                     240
cccacgaaac actaataaaa accacagaga ccagcctg
                                                                     278
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      <211> 121
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      <213> Homo sapien
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      <221> misc_feature
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      <211> 350
      <212> DNA
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                                                                      120
aaacttgata cttttgttct aagtaggaac tagtatacag tncctaggan tggtactcca
                                                                      180
gggtgcccc caactcctgc agccgctcct ctgtgccagn ccctgnaagg aactttcgct
                                                                      240
ccacctcaat caagccctgg gccatgctac ctgcaattgg ctgaacaaac gtttgctgag
                                                                      300
ttcccaagga tgcaaagcct ggtgctcaac tcctggggcg tcaactcagt
                                                                      350
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      <211> 399
<212> DNA
                                            3 , 1 . T T
      <213> Homo sapien
                                 in the contract and the second of the
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      <221> misc feature
      <222> (1)...(399)
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gcagacttgt gtctgccttc aanaagccag acaggaaggc cctgcctgcc ttggctctga
                                                                      180
cctggcggcc agccagccag ccacaggtgg gcttcttcct tttgtggtga caacnccaag
                                                                      240
aaaactgcag aggcccaggg tcaggtgtna gtgggtangt gaccataaaa caccaggtgc
                                                                      300
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teccaggaac cegggeaaag gecateeeca cetacageca geatgeecac tggegtgatg
                                                                                                                                                                                                                                                                                               360
         ggtgcagang gatgaagcag ccagntgttc tgctgtggt
                                                                                                                                                                                                                                                                                               399
                                                                                                en
                                 <210> 137
                                <211> 165
<212> DNA
 and in the
                                <213> Homo sapien
                                                                                                                                    ** :
                                <220>
                                <221> misc_feature
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                                 <222> (1)...(165)
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        ggaggaagtg tgtgaacgta gggatgtaga ngttttggcc gtgctaaatg agcttcggga
        ttggctggtc ccactggtgg tcactgtcat tggtggggtt cctgt
                                <210> 138
                       <211> 338
                               <212> DNA data a graft same in the design of the programme.
                                                                                                                                                                                                                                      Company of the Company of the
                               <213> Homo sapien > 2037 | 1.83 | 0.13 | 1.84
                               <220>
                               <221> misc feature
                               <222> (1)...(338)
                               <223> n = A, T, C or G
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       ttaacttctc cagtaagaat cagggacttg aaatggaaac gttaacagcc acatgcccaa
       tgctgggcag tctcccatgc cttccacagt gaaagggctt gagaaaaatc acatccaatg
                                                                                                                                                                                                                                                                                            180
       tcatgtgttt ccagccacac caaaaggtgc ttggggtgga gggctggggg catananggt
       cangceteag gaageeteaa gtteeattea getttgeeae tgtacattee ceatntttaa
       aaaaactgat gccttttttt tttttttttg taaaattc
                                                                                                                                                                                                                                          338
     M. (2)
                            <213>. Homo sapien state parties of the same state of the same sta
                              <400> 139
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      gaaagggact tcgagtaaga aggtgattta cagccagcct agtgcccgaa gtgaaggaga
                                                                                                                                                                                                                                                                                           120
      attcaaacag acctcgtcat tectggtgtg agectggtcg getcacegee tatcatetge
                                                                                                                                                                                                                                                                                           180
      atttgcctta ctcaggtgct accggactct ggcccctgat gtctgtagtt tcacaggatg
                                                                                                                                                                                                                                                                                           240
      cettatttgt ettetacace ceacagggee ecetaettet teggatgtgt ttttaataat
                                                                                                                                                                                                                                                                                           300
     gtcagctatg tgccccatcc tccttcatgc cctccctccc tttcctacca ctgctgagtg
                                                                                                                                                                                                                                                                                           360
      gcctggaact tgtttaaagt gt
                                                                                                                                                                                                         382
                                                                                                                                                                                                         <210> 140
                             <211> 200
                            <212> DNA
                            <213> Homo sapiene cate cases and a particular section of the same specific and sections and the same section of the same sect
                                                    ាយមាន នេះ ក្រុមក្រុង ខេត្តស្ថា មានដែលប្រធានមន្ត ៤០ ស្គ្រាប់ ប្រើសារប្រជាពលរបស់ មានប្រជាពលរបស់
                           <220> regular of State of notice of good and state of the good of continue
<221> misc_feature good door good of the notice of the good of the goo
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<210> 144 <211> 164

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gcaggacage tateataagt eggeeeagge atceagatae taccatttgt ataaacttea
                                                                                                               180
gtagggagt ccatccaagt gacaggtcta atcaaaggag gaaatggaac ataagcccag tagtaaaatn ttgcttagct gaaacagcca caaaagactt accgccgtgg tgattaccat
                                                                                                               240
                                                                                                               300
caa
                                                                                1 4 - 45 CONT OF STAN
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         <211> 327
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                                                                                                               120
ccaagtcagg gctgggattt gtttcctttc cacattctag caacaatatg ctggccactt cctgaacagg gagggtggga ggagccagca tggaacaagc tgccactttc taaagtagcc
                                                                                                               180
                                                                                                               240
agacttgccc ctgggcctgt cacacctact gatgaccttc tgtgcctgca ggatggaatg
                                                                                                               300
taggggtgag ctgtgtgact ctatggt
                                                                                                               327
                                                                                             4 (4) 4 (4)
         <210> 147
         <211> 173
         <212> DNA
         <213> Homo sapien '

                                                                                    law treet to legan.
         <221> misc_feature
         <222> (1)...(173)
         \langle 223 \rangle n = A, T, C or G
                                                                                              835 835 E
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| • •                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                       |                                                      |                                                      | -                                      |                   |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|------------------------------------------------------|------------------------------------------------------|----------------------------------------|-------------------|
| <400> 147                                                                                                                                                                                                                                                                                                                                                                                                                                                          | ,                                                                                                     |                                                      |                                                      |                                        | •                 |
| acattgtttt tttgagataa a                                                                                                                                                                                                                                                                                                                                                                                                                                            | gcattgana                                                                                             | gagetetect                                           | taacqtqaca                                           | caatggaagg                             | 60                |
| actggaacac atacccacat c                                                                                                                                                                                                                                                                                                                                                                                                                                            | ++++++                                                                                                | aggastaatt                                           | ttctcataaa                                           | atcttactat                             | 120               |
| actggaacac atacccacat c                                                                                                                                                                                                                                                                                                                                                                                                                                            | culgulary                                                                                             | ayyyacaacc                                           | thetesanta                                           | ~++                                    | 173               |
| atattcaagc acatatgtta t                                                                                                                                                                                                                                                                                                                                                                                                                                            | atattattc                                                                                             | agttccatgt                                           | ttatageeta                                           | gcc                                    | 113               |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                       |                                                      |                                                      |                                        |                   |
| <210> 148                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                       |                                                      |                                                      |                                        | *                 |
| <211> 477                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                       |                                                      |                                                      |                                        |                   |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                       |                                                      |                                                      |                                        |                   |
| <212> DNA                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                       |                                                      |                                                      |                                        |                   |
| <213> Homo sapien                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 1                                                                                                     |                                                      |                                                      | •                                      |                   |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                       |                                                      |                                                      | *                                      |                   |
| <220>                                                                                                                                                                                                                                                                                                                                                                                                                                                              | ,                                                                                                     |                                                      |                                                      |                                        |                   |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | *                                                                                                     |                                                      |                                                      |                                        |                   |
| <221> misc_featur                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                       |                                                      |                                                      |                                        |                   |
| <222> (1)(477)                                                                                                                                                                                                                                                                                                                                                                                                                                                     | •                                                                                                     |                                                      |                                                      |                                        |                   |
| <223> n = A, T, C c                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                       |                                                      |                                                      |                                        |                   |
| 1220, 11 11/1/0                                                                                                                                                                                                                                                                                                                                                                                                                                                    | _                                                                                                     |                                                      |                                                      |                                        |                   |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                       |                                                      | ,                                                    |                                        |                   |
| <400> 148                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                       | _                                                    |                                                      |                                        | 60                |
| acaaccactt tatctcatcg a                                                                                                                                                                                                                                                                                                                                                                                                                                            | atttttaac                                                                                             | ccaaactcac                                           | tcactgtgcc                                           | tttctatcct                             | 60                |
| atgggatata ttatttgatg                                                                                                                                                                                                                                                                                                                                                                                                                                              | ctccatttca                                                                                            | tcacacatat                                           | atgaataata                                           | cactcatact                             | 120               |
| gccctactac ctgctgcaat a                                                                                                                                                                                                                                                                                                                                                                                                                                            | atcacattc                                                                                             | cetteetate                                           | ctgaccctga                                           | agccattggg                             | 180               |
| geoclaciae elgelgeaal a                                                                                                                                                                                                                                                                                                                                                                                                                                            | Lacoacacic                                                                                            | coccoccacc                                           | aattasaata                                           | catteetese                             | 240               |
| gtggtcctag tggccatcag t                                                                                                                                                                                                                                                                                                                                                                                                                                            | ccangeetg                                                                                             | caccurgage                                           | Colligagete                                          | Cattyctcat                             |                   |
| nccancccac ctcaccgacc                                                                                                                                                                                                                                                                                                                                                                                                                                              | ccatcctctt                                                                                            | acacagetae                                           | ctccttgctc                                           | tctaacccca                             | 300               |
| tagattatnt ccaaattcag t                                                                                                                                                                                                                                                                                                                                                                                                                                            | tcaattaaqt                                                                                            | tactattaac                                           | actctacccg                                           | acatgtccag                             | 360               |
| caccactggt aagccttctc                                                                                                                                                                                                                                                                                                                                                                                                                                              | ranccaacac                                                                                            | acacacacac                                           | acacncacac                                           | acacacatat                             | 420               |
| ccaggcacag gctacctcat                                                                                                                                                                                                                                                                                                                                                                                                                                              | -ttta                                                                                                 | aggggtttaa                                           | ttaccatoct                                           | atootoo                                | 477               |
| ccaggcacag gctacctcat c                                                                                                                                                                                                                                                                                                                                                                                                                                            | Cilcacaacc                                                                                            | accecteda                                            | ccaccacgoc                                           | acggegg                                | -                 |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                       | * : * *                                              |                                                      |                                        |                   |
| <210> 149                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                       |                                                      |                                                      |                                        |                   |
| <211> 207                                                                                                                                                                                                                                                                                                                                                                                                                                                          | and the second                                                                                        |                                                      |                                                      |                                        |                   |
| <212> DNA                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                       |                                                      | 1                                                    | The second second                      |                   |
| CAIAN DINA                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                       | • "                                                  |                                                      |                                        |                   |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                       |                                                      |                                                      | * .                                    |                   |
| <213> Homo sapier                                                                                                                                                                                                                                                                                                                                                                                                                                                  | n '                                                                                                   | •                                                    |                                                      | ** *                                   | •                 |
| <213> Homo sapier                                                                                                                                                                                                                                                                                                                                                                                                                                                  | n.                                                                                                    | •                                                    |                                                      |                                        |                   |
| <213> Homo sapier                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                       | •                                                    |                                                      |                                        |                   |
| <213> Homo sapier                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                       | ttgcaatgag                                           | agcatttaag                                           | agggaagaac                             | 60                |
| <213> Homo sapier <400> 149 acagttgtat tataatatca a                                                                                                                                                                                                                                                                                                                                                                                                                | agaaataaac                                                                                            | ttgcaatgag                                           | agcatttaag                                           | agggaagaac<br>ggtggggct                |                   |
| <pre>&lt;213&gt; Homo sapier &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a</pre>                                                                                                                                                                                                                                                                                                                                                                 | agaaataaac<br>aggaaggttt                                                                              | ctgtggggag                                           | tgggatgtaa                                           | ggtggggcct                             | 120               |
| <pre>&lt;213&gt; Homo sapier  &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc</pre>                                                                                                                                                                                                                                                                                                                                          | agaaataaac<br>aggaaggttt<br>caggtaagtg                                                                | ctgtggggag                                           | tgggatgtaa                                           | ggtggggcct                             | 120<br>180        |
| <pre>&lt;213&gt; Homo sapier  &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc</pre>                                                                                                                                                                                                                                                                                                                                          | agaaataaac<br>aggaaggttt<br>caggtaagtg                                                                | ctgtggggag                                           | tgggatgtaa                                           | ggtggggcct                             | 120               |
| <pre>&lt;213&gt; Homo sapier &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a</pre>                                                                                                                                                                                                                                                                                                                                                                 | agaaataaac<br>aggaaggttt<br>caggtaagtg                                                                | ctgtggggag                                           | tgggatgtaa                                           | ggtggggcct                             | 120<br>180        |
| <pre>&lt;213&gt; Homo sapier</pre>                                                                                                                                                                                                                                                                                                                                                                                                                                 | agaaataaac<br>aggaaggttt<br>caggtaagtg                                                                | ctgtggggag                                           | tgggatgtaa                                           | ggtggggcct                             | 120<br>180        |
| <pre>&lt;213&gt; Homo sapier     &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a &lt;210&gt; 150</pre>                                                                                                                                                                                                                                                                                             | agaaataaac<br>aggaaggttt<br>caggtaagtg                                                                | ctgtggggag                                           | tgggatgtaa                                           | ggtggggcct                             | 120<br>180        |
| <pre>&lt;213&gt; Homo sapier     &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a &lt;210&gt; 150     &lt;211&gt; 111</pre>                                                                                                                                                                                                                                                                         | agaaataaac<br>aggaaggttt<br>caggtaagtg                                                                | ctgtggggag                                           | tgggatgtaa                                           | ggtggggcct                             | 120<br>180        |
| <pre>&lt;213&gt; Homo sapier     &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a &lt;210&gt; 150</pre>                                                                                                                                                                                                                                                                                             | agaaataaac<br>aggaaggttt<br>caggtaagtg                                                                | ctgtggggag                                           | tgggatgtaa                                           | ggtggggcct                             | 120<br>180        |
| <pre>&lt;213&gt; Homo sapier     &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a &lt;210&gt; 150     &lt;211&gt; 111</pre>                                                                                                                                                                                                                                                                         | agaaataaac<br>aggaaggttt<br>caggtaagtg<br>agtgaaa                                                     | ctgtggggag                                           | tgggatgtaa                                           | ggtggggcct                             | 120<br>180        |
| <pre>&lt;213&gt; Homo sapier     &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a  &lt;210&gt; 150     &lt;211&gt; 111     &lt;212&gt; DNA</pre>                                                                                                                                                                                                                                                    | agaaataaac<br>aggaaggttt<br>caggtaagtg<br>agtgaaa                                                     | ctgtggggag                                           | tgggatgtaa                                           | ggtggggcct                             | 120<br>180        |
| <pre>&lt;213&gt; Homo sapier &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a &lt;210&gt; 150 &lt;211&gt; 111 &lt;212&gt; DNA &lt;213&gt; Homo sapier</pre>                                                                                                                                                                                                                                         | agaaataaac<br>aggaaggttt<br>caggtaagtg<br>agtgaaa                                                     | ctgtggggag                                           | tgggatgtaa                                           | ggtggggcct                             | 120<br>180        |
| <pre>&lt;213&gt; Homo sapier &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a  &lt;210&gt; 150 &lt;211&gt; 111 &lt;212&gt; DNA &lt;213&gt; Homo sapier &lt;220&gt;</pre>                                                                                                                                                                                                                            | agaaataaac<br>aggaaggttt<br>caggtaagtg<br>agtgaaa<br>n                                                | ctgtggggag                                           | tgggatgtaa                                           | ggtggggcct                             | 120<br>180        |
| <pre>&lt;213&gt; Homo sapier &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a  &lt;210&gt; 150 &lt;211&gt; 111 &lt;212&gt; DNA &lt;213&gt; Homo sapier &lt;220&gt; &lt;221&gt; misc_featur</pre>                                                                                                                                                                                                    | agaaataaac<br>aggaaggttt<br>caggtaagtg<br>agtgaaa<br>n                                                | ctgtggggag                                           | tgggatgtaa                                           | ggtggggcct                             | 120<br>180        |
| <pre>&lt;213&gt; Homo sapier &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a  &lt;210&gt; 150 &lt;211&gt; 111 &lt;212&gt; DNA &lt;213&gt; Homo sapier &lt;220&gt;</pre>                                                                                                                                                                                                                            | agaaataaac<br>aggaaggttt<br>caggtaagtg<br>agtgaaa<br>n                                                | ctgtggggag                                           | tgggatgtaa                                           | ggtggggcct                             | 120<br>180        |
| <pre>&lt;213&gt; Homo sapier &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a  &lt;210&gt; 150 &lt;211&gt; 111 &lt;212&gt; DNA &lt;213&gt; Homo sapier &lt;220&gt; &lt;221&gt; misc_featur &lt;222&gt; (1)(111</pre>                                                                                                                                                                                | agaaataaac<br>aggaaggttt<br>caggtaagtg<br>agtgaaa<br>n<br>re<br>)                                     | ctgtggggag                                           | tgggatgtaa                                           | ggtggggcct                             | 120<br>180        |
| <pre>&lt;213&gt; Homo sapier &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a  &lt;210&gt; 150 &lt;211&gt; 111 &lt;212&gt; DNA &lt;213&gt; Homo sapier &lt;220&gt; &lt;221&gt; misc_featur</pre>                                                                                                                                                                                                    | agaaataaac<br>aggaaggttt<br>caggtaagtg<br>agtgaaa<br>n<br>re<br>)                                     | ctgtggggag                                           | tgggatgtaa<br>tatgggcaca                             | gtgaagaaca                             | 120<br>180<br>207 |
| <pre>&lt;213&gt; Homo sapier &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a  &lt;210&gt; 150 &lt;211&gt; 111 &lt;212&gt; DNA &lt;213&gt; Homo sapier  &lt;220&gt; &lt;221&gt; misc_featu &lt;222&gt; (1)(111 &lt;223&gt; n = A,T,C</pre>                                                                                                                                                          | agaaataaac<br>aggaaggttt<br>caggtaagtg<br>agtgaaa<br>n<br>re<br>)                                     | ctgtggggag                                           | tgggatgtaa<br>tatgggcaca                             | ggtggggcct                             | 120<br>180<br>207 |
| <pre>&lt;213&gt; Homo sapier &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a  &lt;210&gt; 150 &lt;211&gt; 111 &lt;212&gt; DNA &lt;213&gt; Homo sapier  &lt;220&gt; &lt;221&gt; misc_featu &lt;222&gt; (1)(111 &lt;223&gt; n = A,T,C</pre> <400> 150                                                                                                                                                | agaaataaac<br>aggaaggttt<br>caggtaagtg<br>agtgaaa<br>n<br>re<br>)<br>or G                             | ctgtggggag<br>ggtggtgtgg                             | tgggatgtaa<br>tatgggcaca                             | ggtggggcct                             | 120<br>180<br>207 |
| <pre>&lt;213&gt; Homo sapier &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a  &lt;210&gt; 150 &lt;211&gt; 111 &lt;212&gt; DNA &lt;213&gt; Homo sapier  &lt;220&gt; &lt;221&gt; misc_featu &lt;222&gt; (1)(111 &lt;223&gt; n = A,T,C a <!--400--> 150 accttgattt cattgctgct</pre>                                                                                                                   | agaaataaac<br>aggaaggttt<br>caggtaagtg<br>agtgaaa<br>n<br>re<br>)<br>or G                             | ctgtggggag<br>ggtggtgtgg                             | tgggatgtaa<br>tatgggcaca                             | ggtggggcct<br>gtgaagaaca               | 120<br>180<br>207 |
| <pre>&lt;213&gt; Homo sapier &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a  &lt;210&gt; 150 &lt;211&gt; 111 &lt;212&gt; DNA &lt;213&gt; Homo sapier  &lt;220&gt; &lt;221&gt; misc_featu &lt;222&gt; (1)(111 &lt;223&gt; n = A,T,C a <!--400--> 150 accttgattt cattgctgct</pre>                                                                                                                   | agaaataaac<br>aggaaggttt<br>caggtaagtg<br>agtgaaa<br>n<br>re<br>)<br>or G                             | ctgtggggag<br>ggtggtgtgg                             | taggatgtaa<br>tatgggcaca                             | ggtggggcct<br>gtgaagaaca               | 120<br>180<br>207 |
| <pre>&lt;213&gt; Homo sapier &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a  &lt;210&gt; 150 &lt;211&gt; 111 &lt;212&gt; DNA &lt;213&gt; Homo sapier  &lt;220&gt; &lt;221&gt; misc_featu &lt;222&gt; (1)(111 &lt;223&gt; n = A,T,C</pre> <400> 150                                                                                                                                                | agaaataaac<br>aggaaggttt<br>caggtaagtg<br>agtgaaa<br>n<br>re<br>)<br>or G                             | ctgtggggag<br>ggtggtgtgg                             | taggatgtaa<br>tatgggcaca<br>taatttagct<br>catctttggg | ggtggggcct<br>gtgaagaaca<br>aaaacatggg | 120<br>180<br>207 |
| <pre>&lt;213&gt; Homo sapier  &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a  &lt;210&gt; 150 &lt;211&gt; 111 &lt;212&gt; DNA &lt;213&gt; Homo sapier  &lt;220&gt; &lt;221&gt; misc_featur &lt;222&gt; (1)(111 &lt;223&gt; n = A,T,C</pre> <400> 150 accttgattt cattgctgct cacttaaatg tggtcagtgt                                                                                                  | agaaataaac<br>aggaaggttt<br>caggtaagtg<br>agtgaaa<br>n<br>re<br>)<br>or G                             | ctgtggggag<br>ggtggtgtgg                             | taggatgtaa<br>tatgggcaca<br>taatttagct               | ggtggggcct<br>gtgaagaaca<br>aaaacatggg | 120<br>180<br>207 |
| <pre>&lt;213&gt; Homo sapier &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a  &lt;210&gt; 150 &lt;211&gt; 111 &lt;212&gt; DNA &lt;213&gt; Homo sapier  &lt;220&gt; &lt;221&gt; misc_featur &lt;222&gt; (1)(111 &lt;223&gt; n = A,T,C</pre> <400> 150 accttgattt cattgctgct cacttaaatg tggtcagtgt <210> 151                                                                                         | agaaataaac<br>aggaaggttt<br>caggtaagtg<br>agtgaaa<br>n<br>re<br>)<br>or G                             | ctgtggggag<br>ggtggtgtgg                             | taggatgtaa<br>tatgggcaca<br>taatttagct               | ggtggggcct<br>gtgaagaaca<br>aaaacatggg | 120<br>180<br>207 |
| <pre>&lt;213&gt; Homo sapier &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a  &lt;210&gt; 150 &lt;211&gt; 111 &lt;212&gt; DNA &lt;213&gt; Homo sapier  &lt;220&gt; &lt;221&gt; misc_featu &lt;222&gt; (1)(111 &lt;223&gt; n = A,T,C  &lt;400&gt; 150 accttgattt cattgctgct cacttaaatg tggtcagtgt  &lt;210&gt; 151 &lt;211&gt; 196</pre>                                                            | agaaataaac<br>aggaaggttt<br>caggtaagtg<br>agtgaaa<br>n<br>re<br>)<br>or G                             | ctgtggggag<br>ggtggtgtgg                             | taggatgtaa<br>tatgggcaca<br>taatttagct               | ggtggggcct<br>gtgaagaaca<br>aaaacatggg | 120<br>180<br>207 |
| <pre>&lt;213&gt; Homo sapier &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a  &lt;210&gt; 150 &lt;211&gt; 111 &lt;212&gt; DNA &lt;213&gt; Homo sapier  &lt;220&gt; &lt;221&gt; misc_featur &lt;222&gt; (1)(111 &lt;223&gt; n = A,T,C</pre> <400> 150 accttgattt cattgctgct cacttaaatg tggtcagtgt <210> 151                                                                                         | agaaataaac<br>aggaaggttt<br>caggtaagtg<br>agtgaaa<br>n<br>re<br>)<br>or G                             | ctgtggggag<br>ggtggtgtgg                             | taggatgtaa<br>tatgggcaca<br>taatttagct               | ggtggggcct<br>gtgaagaaca<br>aaaacatggg | 120<br>180<br>207 |
| <pre>&lt;213&gt; Homo sapier &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a  &lt;210&gt; 150 &lt;211&gt; 111 &lt;212&gt; DNA &lt;213&gt; Homo sapier  &lt;220&gt; &lt;221&gt; misc_featu &lt;222&gt; (1)(111 &lt;223&gt; n = A,T,C</pre> <400> 150 accttgattt cattgctgct cacttaaatg tggtcagtgt  <210> 151 <211> 196 <212> DNA <213> Homo sapier                                                   | agaaataaac<br>aggaaggttt<br>caggtaagtg<br>agtgaaa<br>n<br>re<br>)<br>or G<br>ctgatggaaa<br>ttggacttgt | ctgtggggag<br>ggtggtgtgg<br>cccaactato<br>taactantgg | tgggatgtaa<br>tatgggcaca<br>taatttagct               | ggtggggcct<br>gtgaagaaca<br>aaaacatggg | 120<br>180<br>207 |
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| <pre>&lt;213&gt; Homo sapier &lt;400&gt; 149 acagttgtat tataatatca a taacgtattt tagagagcca a gatgataaat aagagtcagc a tttcaggcag agggaacagc a  &lt;210&gt; 150 &lt;211&gt; 111 &lt;212&gt; DNA &lt;213&gt; Homo sapier  &lt;220&gt; &lt;221&gt; misc_featu &lt;222&gt; (1)(111 &lt;223&gt; n = A,T,C</pre> <pre>&lt;400&gt; 150 accttgattt cattgctgct cacttaaatg tggtcagtgt</pre> <pre>&lt;20&gt; 151 &lt;211&gt; 196 &lt;212&gt; DNA &lt;213&gt; Homo sapier</pre> | agaaataaac<br>aggaaggttt<br>caggtaagtg<br>agtgaaa<br>n<br>re<br>)<br>or G<br>ctgatggaaa<br>ttggacttgt | ctgtggggag<br>ggtggtgtgg<br>cccaactato<br>taactantgg | taggatgtaa<br>tatgggcaca<br>taatttagct               | ggtggggcct<br>gtgaagaaca<br>aaaacatggg | 120<br>180<br>207 |
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agcaagatgg ctttgaactc agggtcacca ccagctattg gaccttacta tgaaaaccat 120 ggataccaac cggaaaaccc ctatcccgca cagcccactg tggtccccac tgtctacgag 180 gtgcatccgg ctcagt 196 <210> 152 Gradier State und du <211> 132 <212> DNA <213> Homo sapien <400> 152 acagcacttt cacatgtaag aagggagaaa ttcctaaatg taggagaaag ataacagaac 60 cttccccttt tcatctagtg gtggaaacct gatgctttat gttgacagga atagaaccag 🕾 120 ing the figure of the gagggagttt gt 132 3 1 2 2 . . . . . . . . . . . **<**210> 153 <211> 285 <212> DNA <213> Homo sapien product section of the control of . 🚁 🤃 3.2  $1.5 \pm 0.0$ . : ; acaanaccca nganaggcca ctggccgtgg tgtcatggcc tccaaacatg aaagtgtcag cttctgctct tatgtcctca tctgacaact ctttaccatt tttatcctcg ctcagcagga 120 gcacatcaat aaagtccaaa gtcttggact tggccttggc ttggaggaag tcatcaacac 180 cctggctagt gagggtgcgg cgccgctcct ggatgacggc atctgtgaag tcgtgcacca 240 gtctgcaggc cctgtggaag cgccgtccac acggagtnag gaatt gaarte garee same 285 <210> 154 100 0000 accacagtcc tgttgggcca gggcttcatg accctttctg tgaaaagcca tattatcacc 60 accecaaatt ttteettaaa tatetttaae tgaaggggte ageetettga etgeaaagae 120 ectaageegg ttacacaget aacteccact ggeeetgatt tgtgaaattg etgetgeetg 180 attggcacag gagtcgaagg tgttcagctc ccctcctccg tggaacgaga ctctgatttg 240 agtttcacaa attctcgggc cacctcgtca ttgctcctct gaaataaaat ccggagaatg 300 gtcaggcctg tctcatccat atggatcttc cgg 333 <210> 155 <211> 308 <212> DNA <213> Homo sapien processors of side of side of sections of the section of the secti <221> misc\_feature <222> (1)...(308) <223> n = A, T, C or G<400> 155 actggaaata ataaaaccca catcacagtg ttgtgtcaaa gatcatcagg gcatggatgg gaaagtgett tgggaactgt aaagtgeeta acacatgate gatgattttt gttataatat 🚁 ttgaatcacg gtgcatacaa actotoctgc ctgctcctcc tgggccccag ccccagcccc 180

| atcacagete aetgetetgt teatecagge ceageatgta gtggetgatt ettettgget gettttagee tecanaagtt tetetgaage caaceaaace tetangtgta aggeatgetg geeetggt  240 300                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |  |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
| <210> 156<br><211> 295<br><212> DNA<br><213> Homo sapien                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |  |
| <400> 156                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |  |
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| gaataggaga ttatgtttgg ccctcatatt ctctcctatc ctccttgcct cattctatgt 180                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |  |
| ctaatatatt ctcaatcaaa taaggttagc ataatcagga aatcgaccaa ataccaatat 240                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |  |
| aaaaccagat gtctatcctt aagattttca aatagaaaac aaattaacag actat 295                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |  |
| <210> 157                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |  |
| <211> 126                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |  |
| <212> DNA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |  |
| <213> Homo sapien'                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |  |
| <400> 157                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |  |
| acaagtttaa atagtgctgt cactgtgcat gtgctgaaat gtgaaatcca ccacatttct 60                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  |
| gaagagcaaa acaaattotg toatgtaato totatottgg gtogtgggta tatotgtooc 120 ottagt 126                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |  |
| The state of the s |  |
| <210> 158                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |  |
| <211> 442<br><212> DNA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |  |
| <213> Homo sapien                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |  |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |
| <220> <221> misc_feature                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |  |
| <222> misc_leature                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |  |
| $\langle 223 \rangle$ n = A,T,C or G                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |
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| aanccagcag getgeeeeta gteagteett eetteeagag aaaaagagat ttgagaaagt 120                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |  |
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| nacagacggg ctctttgcag agccgggact ctgagangga catgagggce tctgcctctg 420                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |  |
| tottcattet etgatoteet ot 442                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |  |
| <210> 159                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |  |
| <211> 498                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |  |
| <212> DNA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |  |
| <213> Homo sapien                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |  |
| <220>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |  |
| <221> misc feature                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |  |
| <222> (1)(498)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |  |
| $\langle 223 \rangle$ n = A,T,C or G                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  |
| <400> 159                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |  |
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                                                                                                                                                       180
cactagacat cteatcagcc acttgtgtga agagatgccc catgacccca gatgcctctc
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                                                                                                                                                      300
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<213> Homo sapien

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catttataca gacaggegtg aagacattca cgacaaaaac gcgaaattct atcccgtgac
                                                                                                                                                 60
canagaagge agctacgget actectaeat cetggcgtgg gtggcetteg cetgeacett
                                                                                                                                                120
                                                                                                                                                137
catcagcggc atgatgt
            <210> 164
            <211> 469
            <212> DNA
            <213> Homo sapien
            <220>
            <221> misc feature
            <222> (1)...(469)
            <223> n = A, T, C or G
           <400> 164
cttatcacaa tgaatgttct cctgggcagc gttgtgatct ttgccacctt cgtgacttta
tgcaatgcat catgctattt catacctaat gagggagttc caggagattc aaccaggaaa
                                                                                                                                                120
tgcatggatc tcaaaggaaa caaacaccca ataaactcgg agtggcagac tgacaactgt
                                                                                                                                                180
gagacatgca cttgctacga aacagaaatt tcatgttgca cccttgtttc tacacctgtg
                                                                                                                                                240
ggttatgaca aagacaactg ccaaagaatc ttcaagaagg aggactgcaa gtatatcgtg
                                                                                                                                                300
qtqqaqaaga aqqacccaaa aaaqacctqt tctqtcaqtq aatqqataat ctaatqtqct
                                                                                                                                                360
totaqtaqqc acaqqqctcc caqqccaqqc ctcattctcc tctqqcctct aataqtcaat
                                                                                                                                                420
gattgtgtag ccatgcctat cagtaaaaag atntttgagc aaacacttt
                                                                                                                                                469
            <210> 165
            <211> 195
            <212> DNA
            <213> Homo sapien
            <221> misc_feature
<222> (1)...(195)
            <223> n = A,T,C or G
acaqtttttt atanatatcq acattqccqq cacttqtgtt cagtttcata aagctggtgg
                                                                                                                                                 60
                                                                                                                                                120
atcogctqtc atcoactatt ccttqqctaq aqtaaaaatt attcttatag cccatqtccc
                                                                                                                                                180
tgcaggccgc ccgcccgtag ttctcgttcc agtcgtcttg gcacacaggg tgccaggact
                                                                                                                                                195
tcctctqaga tqagt
            <210> 166
            <211> 383
            <212> DNA
            <213> Homo sapien
            <220>
                                                         and the second of the second o
            <221> misc_feature
            <222> (1)...(383)
            <223> n = A,T,C or G
                                                                    lan eren la conque o roma de mitro angré de dibie
            <400> 166
                                                              acatcttagt agtgtggcac atcaggggc catcagggtc acagtcactc atagcctcgc
                                                                                                                                                60
cgaggtcgga gtccacacca ccggtgtagg tgtgctcaat cttgggcttg gcgcccacct
                                                                                                                                               120
ttggagaagg gatatgetge acacacatgt ccacaaagee tgtgaacteg ccaaagaatt
                                                                                                                                                180
tttgcagacc agectgagca aggggeggat gttcagette ageteeteet tegtcaggtg
                                                                                                                                                240
gatgccaacc tcgtctangg tccgtgggaa gctggtgtcc acntcaccta caacctgggc
                                                                                                                                                300
gangatetta taaagagget eenagataaa etecaegaaa ettetetggg agetgetagt
                                                                                                                                                360
                                                                                                                                                383
nggggccttt ttggtgaact ttc
```

```
<210> 167
                                     <211> 247
                                      <212> DNA
                                      <213> Homo sapien
                                     <220>
                                     <221> misc feature
                                     <222> (1) ... (247)
                                     <223> n = A, T, C or G
                                     <400> 167
           acagagecag acettggeca taaatgaane agagattaag actaaacece aagteganat
           tggagcagaa actggagcaa gaagtgggcc tggggctgaa gtagagacca aggccactgc
           tatanccata cacagagcca acteteagge caaggenatg gttggggcag anceagagae
          tcaatctgan tccaaagtgg tggctggaac actggtcatg acanaggcag tgactctgac 240
grading space to build the production
                                     <220>
                                     <221> misc_feature
                                     <222> (1)...(273)
                                     \langle 223 \rangle n = A, T, C or G
                                     <400> 168
           acttctaagt tttctagaag tggaaggatt gtantcatcc tgaaaatggg tttacttcaa
                                                                                                                                                                                                                                                                                                                          60
           aatccctcan ccttgttctt cacnactgtc tatactgana gtgtcatgtt tccacaaagg
                                                                                                                                                                                                                                                                                                                      120
           gctgacacct gagcctgnat tttcactcat ccctgagaag ccctttccag tagggtgggc
                                                                                                                                                                                                                                                                                                                      180
           aattoccaac ttocttgcca caagettocc aggetttete coctggaaaa ctocagettg
                                                                                                                                                                                                                                                                                                                      240
          agteceagat acacteatgg detgeeetgg gea
                                                                                                                                                                                                                                                                                                                     273
                                    <210> 169
                                    <211> 431
                                                                                                . = 1 -
                                    <212> DNA
                                    <213> Homo sapien
                                    <220>
                                    <221> misc feature
                                    <222> (1)...(431)
                                    <223> n = A, T, C or G
                                    <400> 169
          acagocttgg cttccccaaa ctccacagtc tcagtgcaga aagatcatct tccagcagtc
                                                                                                                                                                                                                                                                                                                         60
          ageteagace agggteaaag gatgtgacat caacagttte tggttteaga acaggtteta
                                                                                                                                                                                                                                                                                                                     120
          ctactgtcaa atgaccccc atacttcctc aaaggctgtg gtaagttttg cacaggtgag
                                                                                                                                                                                                                                                                                                                    180
          ggcagcagaa agggggtant tactgatgga caccatcttc tctgtatact ccacactgac
                                                                                                                                                                                                                                                                                                                     240
          cttgccatgg gcaaaggccc ctaccacaaa aacaatagga tcactgctgg gcaccagctc
          acgcacatca ctgacaaccg ggatggaaaa agaantgcca actttcatac atccaactgg ...... 360.
          aaagtgatet gatactggat tettaattae etteaaaage ttetggggge cateagetge 420
         togaacactg a way and a specific and service and the specific speci
                                   <210> 170 (1) (2000) 713 h (2000) 646 (1) 930 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 (200) 200 
                                                                                  which are some considered to suggest that the second of the second constant \sigma
                                    <211> 266
                                                                                  on the grands of the contract 
                                    <212> DNA
                                                                                                                                                                                                                          thing triber, logical and avoiding
```

```
<213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (266)
      <223> n = A, T, C or G
      <400> 170
acctgtgggc tgggctgtta tgcctgtgcc ggctgctgaa agggagttca gaggtggagc
                                                                     -60
tcaaggaget etgeaggeat tttgecaane etetecanag canagggage aacetacaet
                                                                    120
ccccgctaga aagacaccag attggagtcc tgggaggggg agttggggtg ggcatttgat
                                                                    180
gtatacttgt cacctgaatg aangagccag agaggaanga gacgaanatg'anattggcct
                                                                    240
tcaaagctag gggtctggca ggtgga
                                                                    266
      <210> 171
      <211> 1248
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(1248)
      <223> n = A, T, C or G
      <400> 171
ggcagccaaa tcataaacgg cgaggactgc agcccgcact cgcagccctg gcaggcggca
                                                                     60
ctggtcatgg aaaacgaatt gttctgctcg ggcgtcctgg tgcatccgca gtgggtgctg
                                                                    120
tcagcegeae actgttteca gaagtgagtg cagageteet acaccategg getgggeetg
                                                                    180
cacagtettg aggeegaeea agageeaggg ageeagatgg tggaggeeag ceteteegta
                                                                    240
cggcacccag agtacaacag accettgete getaacgace teatgeteat caaqttqqae
                                                                    300
gaatccgtgt ccgagtctga caccatccgg agcatcagca ttgcttcgca gtgccctacc
                                                                    360
gcggggaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc
                                                                    420
gtgctgcagt gcgtgaacgt gtcggtggtg tctgaggagg tctgcagtaa gctctatgac
                                                                    480
ccgctgtacc accccagcat gttctgcgcc ggcggagggc aagaccagaa ggactcctgc
aacggtgact ctggggggcc cctgatctgc aacgggtact tgcagggcct tgtgtctttc
                                                                    600
ggaaaagccc cgtgtggcca agttggcgtg ccaggtgtct acaccaacct ctgcaaattc
                                                                    660
actgagtgga tagagaaaac cgtccaggcc agttaactct ggggactggg aacccatgaa
                                                                    720
attgaccccc aaatacatcc tgcggaagga attcaggaat atctgttccc agcccctcct
                                                                   780
ccctcaggcc caggagtcca ggcccccagc ccctcctccc tcaaaccaag ggtacagatc
                                                                   840
cocagococt cotocotoag accoaggagt coagacococ cagococtoc tocotoagac
                                                                    900
ecaggagtec ageceetect eceteagace eaggagteca gacceeceag eceetectee
                                                                  960
ctcagaccca ggggtccagg cccccaaccc ctcctccctc agactcagag gtccaagccc
ccaaccente attecceaga eccagaggte caggteccag eccetentee etcagaccea
geggteeaat gecacetaga etnteeetgt acacagtgee ceettgtgge acgttgacee 1140
aaccttacca gttggttttt catttttngt ccctttcccc tagatccaga aataaagttt: 1200
<210> 172
<211> 159
<212> PRT
<213> Homo sapien
<220>
<221> VARIANT
      <221> VARIANT
      <222> (1)...(159)
      <223> Xaa = Any Amino Acid
      <400> 172
```

```
Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro
                                                                                          10
    Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser
                                20
                                                                                 25
     Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr
                                                                        40
    Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly
                                                              55
Arg Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu
                          The transfer 170 ( ) at Tight and 75 through a feet ( ) at 80 fe
     Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe
                           Cys Ala Gly Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser
                                                                              105
                                                                                                                               110
                                100
     Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe
                                                                                                              125 · 3 · 3
                       115
                                                                       120
     Gly Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn
                                                                                                             140
                                                                                                                          135
     Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
     145
                                                    150
                                                                                                                        1 2 2 2 1
                   <210> 173
                   <211> 1265
                   <212> DNA
                   <213> Homo sapien

- App App to the configuration of promy a application of a configuration of the configu
                   400> 173
    ggcagcccgc actcgcagcc ctggcaggcg gcactggtca tggaaaacga attgttctgc 60
   togggogtoc tggtgcatco gcagtgggtg ctgtcagcog cacactgttt ccagaactco - 120
   tacaccateg ggetgggeet geacagtett gaggeegace aagageeagg gageeagatg 199 180
     gtggaggcca gcctctccgt acggcaccca gagtacaaca gacccttgct cgctaacgac 111 240
ctcatgctca tcaagttgga cgaatccgtg tccgagtctg acaccatccg gagcatcagc 300
 attgcttcgc agtgccctac cgcggggaac tettgcctcg tttctggctg gggtctgctg
 gcgaacggtg agctcacggg tgtgtgtctg ccctcttcaa ggaggtcctc tgcccagtcg
    cgggggctga cccagagctc tgcgtcccag gcagaatgcc taccgtgctg cagtgcgtga 480
acgtgtcggt ggtgtctgag gaggtctgca gtaagctcta tgacccgctg taccacccca
                                                                                                                                                                            540
   gcatgttctg cgccggcgga gggcaagacc agaaggactc ctgcaacggt gactctgggg
                                                                                                                                                                            600
     ggccctgat ctgcaacggg tacttgcagg gccttgtgtc tttcggaaaa gccccgtgtg
     gccaagttgg cgtgccaggt gtctacacca acctctgcaa attcactgag tggatagaga
                                                                                                                                                                           720
    aaaccgtcca ggccagttaa ctctggggac tgggaaccca tgaaattgac ccccaaatac
 atcctgcgga aggaattcag gaatatctgt tcccagcccc tcctccctca ggcccaggag
                                                                                                                                                                            840
     tecaggeece cageceetee teceteaaae caagggtaca gateeceage ceeteetee
                                                                                                                                                                            900
    tragacroag gagtroagar ecccagoro etectroeto agarcragga gtroagroco
                                                                                                                                                                            960
    tecteentea gacceaggag tecagaceee ceageceete eteceteaga eccaggggtt
                                                                                                                                                                          1020
    gaggececca acceptecte etteagagte agaggtecaa geocceaace ectegtteec
                                                                                                                                                                          1080
    cagacccaga ggtnnaggtc ccagcccctc ttccntcaga cccagnggtc caatgccacc
                                                                                                                                                                          1140
    tagattttcc ctgnacacag tgcccccttg tggnangttg acccaacctt accagttggt
                                                                                                                                                                          1200
    ttttcatttt tngtcccttt cccctagatc cagaaataaa gtttaagaga ngngcaaaaa
                                                                                                                                                                          1260
                                                                                                                                     1265
     aaaaa
                                                                                                       glady of the second of the sec
```

<210> 174 <211> 1459 <212> DNA <213> Homo sapien

```
<220>
      <221> misc feature
      <222> (1)...(1459)
      <223> n = A, T, C or G
      <400> 174
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                                                                        60
tgcacagtet tgaggeegae caagageeag ggageeagat ggtggaggee ageeteteeg
                                                                       120
tacggcaccc agagtacaac agaccettge tegetaacga ceteatgete atcaagttgg
                                                                       180
acgaatecgt gteegagtet gaeaceatee ggageateag cattgetteg cagtgeecta
                                                                       240
                                                                       300
ccgcggggaa ctcttgcctc gtttctggct ggggtctgct ggcgaacggt gagctcacgg
gtgtgtgtct gecetettea aggaggteet etgeecagte gegggggetg acceagaget
                                                                       360
ctgcgtccca ggcagaatgc ctaccgtgct gcagtgcgtg aacgtgtcgg tggtgtctga
                                                                       420
ngaggtetge antaagétet atgacceget gtaccacece ancatgttet gegeeggegg
                                                                       480
agggcaagac cagaaggact cetgcaacgt gagagagggg aaaggggagg gcaggegact
                                                                       540
                                                                       600
cagggaaggg tggagaaggg ggagacagag acacacaggg ccgcatggcg agatgcagag
atggagagac acacagggag acagtgacaa ctagagagag aaactgagag aaacagagaa
                                                                       660
ataaacacag gaataaagag aagcaaagga agagagaaac agaaacagac atggggaggc
                                                                       720
agaaacacac acacatagaa atgcagttga ccttccaaca gcatggggcc tgagggcggt
                                                                       780
gacctccacc cadtagaaaa teetettata aettttgaet eeccaaaaac etgactagaa
                                                                       840
atagectact gttgaegggg ageettaeea ataacataaa tagtegattt atgeataegt
                                                                       900
tttatgcatt catgatatac ctttgttgga attttttgat atttctaagc tacacagttc
                                                                       960
gtctgtgaat ttttttaaat tgttgcaact ctcctaaaat ttttctgatg tgtttattga
                                                                      1020
aaaaatccaa gtataagtgg acttgtgcat tcaaaccagg gttgttcaag ggtcaactgt
                                                                      1080
gtacccagag ggaaacagtg acacagattc atagaggtga aacacgaaga gaaacaggaa
                                                                      1140
aaatcaagac totacaaaga ggotgggcag ggtggotcat gcotgtaatc ccagcacttt
                                                                      1200
gggaggcgag gcaggcagat cacttgaggt aaggagttca agaccagcct ggccaaaatg
                                                                      1260
gtgaaateet gtetgtaeta aaaataeaaa agttagetgg atatggtgge aggegeetgt
                                                                      1320
                                                                      1380
aatcccagct acttgggagg ctgaggcagg agaattgctt gaatatggga ggcagaggtt
                                                                      1440
gaagtgagtt gagatcacac cactatactc cagctggggc aacagagtaa gactctgtct
caaaaaaaa aaaaaaaaa
                                                                      1459
      <210> 175
      <211> 1167
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(1167)
      <223> n = A, T, C or G
      <400> 175
gegeageect ggeaggege actggteatg gaaaacgaat tgttetgete gggegteetg.
                                                                        60
gtgcatccgc agtgggtgct gtcagccgca cactgtttcc agaactccta caccatcggg
                                                                       120
                                                                       180
ctgggcctgc acagtcttga ggccgaccaa gagccaggga gccagatggt ggaggccagc
ctctccgtac ggcacccaga gtacaacaga ctcttgctcg ctaacgacct catgctcatc
                                                                       240
aagttggacg aatccgtgtc cgagtctgac accatccgga gcatcagcat tgcttcgcag
                                                                       300
tgecetaccg eggggaacte ttgectegtn tetggetggg gtetgetgge gaacggeaga
                                                                       360
atgectaccg tgctgcactg cgtgaacgtg tcggtggtgt ctgaggangt ctgcagtaag
                                                                       420
ctctatgace egetgtacea ecceageatg ttetgegeeg geggagggea agaceagaag
                                                                       480
qactcctqca acqqtqactc tqqqqqccc ctqatctqca acqqqtactt qcaqqqcctt
                                                                       540
gtgtctttcg gaaaagcccc gtgtggccaa cttggcgtgc caggtgtcta caccaacctc
                                                                       600
tgcaaattca ctgagtggat agagaaaacc gtccagncca gttaactctg gggactggga
                                                                       660
acccatgaaa ttgaccccca aatacatcct gcggaangaa ttcaggaata tctgttccca
                                                                       720
                                                                      780
geocetecte ecteaggee aggagtecag geocecage ectectect caaaccaagg
```

```
gtacagatec ccagececte eteceteaga eccaggagte cagacecece agecectent
 centeagace caggagteca geceetecte enteagacge aggagtecag acceccage
                                                                                                                                            900
 contentecg teagacecag gggtgeagge ecceaacece tenteentea gagteagagg
                                                                                                                                            960
 tecaageeee caaceeteg ttececagae ccagaggtne aggteecage cecteeteee
                                                                                                                                          1020
 teagacecag eggteeaatg ecacetagan tntecetgta eacagtgeec cettgtggea
                                                                                                                                          1080
 ngttgaccca accttaccag ttggtttttc attttttgtc cctttcccct agatccagaa
                                                                                                                                          1140
 ataaagtnta agagaagege aaaaaaa
                                                                                                                                          1167
            <210> 176
<211> 205
<212> PRT
<213> Homo sapien
          <213> Homo sapien
<220>
-<221> VARIANT
            <221> VARIANT
<222> (1)...(205)
             <223> Xaa = Any Amino Acid

    *** (関係の可収) promotion of a substitution of a series of a series
             <400> 176
Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
                        5
                                                                                                 15
                                                                        10
  1
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
 Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
 Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Leu Leu
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
                                                                             · 75°
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
                                                                        90
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met
100 105 110
Pro Thr Val Leu His Cys Val Asn Val Ser Val Val Ser Glu Xaa Val
                                                       120
Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala
                                               135
Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly
                                                                               155
Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys
                               165
                                                                       170
Ala Pro Cys Gly Gln Leu Gly Val Pro Gly Val Tyr Thr Asn Leu Cys.
                                                               185
Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Xaa Ser
                                                       200
           <210> 177
<211> 1119
<212> DNA
<213> Homo sapien
<400> 177
gcgcactcgc agccctggca ggcggcactg gtcatggaaa acgaattgtt ctgctcgggc
gtoctggtgc atcogcagtg ggtgctgtca gccgcacact gtttccagaa ctcctacacc
atcgggctgg gcctgcacag tcttgaggcc gaccaagagc cagggagcca gatggtggag 180 gccagcctct ccgtacggca cccagagtac aacagaccct tgctcgctaa cgacctcatg 240
ctcatcaagt tggacgaatc cgtgtcegag tctgacacca tccggagcat cagcattgct 300
tegeagtgce ctacegeggg gaactettge ctegtttetg getggggtet getggegaac 360
```

the state of Lightness.

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|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|
| *<210> 178 <211> 164 <212> PRT <213> Homo sapien                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |        |
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| Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp  1 10 15                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | :      |
| Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu<br>20 25 30                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |        |
| Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val<br>35 40 45                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |        |
| Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu 50 55 60                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |        |
| Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser 65 70 75 80                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |        |
| Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly 85 90 95                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |        |
| Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Asp Ala Val<br>100 105 110                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |        |
| Ile Ala Ile Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu<br>115 120 125                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |        |
| Ser Gln Pro Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |        |
| Thr Ser Cys Cys Ile Leu Thr Gly Cys Ser Leu Leu Thr Ala Ser                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |        |
| 145 150 155 160 Pro Gly Thr Leu                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |        |
| and the control of th |        |
| 210> 179 (2007) 17 (2007) 2007 (2007) 18 (2007) 18 (2007) 179 (2007) 2007 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18 (2007) 18    | •      |
| <211> 250 mm for the first of the first of the first section of the firs | •      |
| <212>DNA PROBLEM STATE OF THE CONTROL OF THE RESERVE OF THE STATE OF THE PROBLEM STATE OF THE ST |        |
| <213> Homo sapien in the restriction of a second for supersymptom of a second secon    | •      |
| 1 <b>  &lt;400&gt; 179</b>     1   1   1   1   1   1   1   1   1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |        |
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awtgstgara aaattaaaat gttctggtty mactttaaaa araaaaaaaa aaaaaaaaa 🌾
           210>, 183
384
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      gageteggat ecaataatet ttgtetgagg geageacaea tatmeagtge catggmaact
                                                                                                                                                                                                                               60
      ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac
                                                                                                                                                                                                                            120
  atgcytyttt gaytacegtg tgccaagtgc tggtgattct yaacacacyt ccatcccgyt
      cttttgtgga aaaactggca cttktctgga actagcarga catcacttac aaattcaccc
                                                                                                                                                                                                                            240
      acgagacact tgaaaggtgt aacaaagcga ytcttgcatt gctttttgtc cctccggcac
                                                                                                                                                                                                                            300
- cagttgtcaa tactaacccg ctggtttgcc tccatcacat ttgtgatctg tagctctgga
                                                                                                                                                                                                                            360
     tacateteet gacagtactg aagaacttet tettttgttt caaaageare tettggtgee
                                                                                                                                                                                                                            420
      tgttggatca ggttcccatt tcccagtcyg aatgttcaca tggcatattt wacttcccac
                                                                                                                                                                                                                            480
      aaaacattgc gatttgaggc tcagcaacag caaatcctgt tccggcattg gctgcaagag
                                                                                                                                                                                                                            540
     cetegatgta geeggeeage geeaaggeag gegeegtgag ceceaceage ageagaagea
                                                                                                                                                                                                                            600
                                                                                                                                                                                                                            601
                        <210> 193
                        <211> 608
                        <212> DNA
                        <213> Homo sapien
                       <220>
                      <221> misc_feature
     atacagocca natoccacca cgaagatgog cttgttgact gagaacctga tgoggtcact
                                                                                                                                                                                                                              60
     ggtcccgctg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcytt
                                                                                                                                                                                                                           120
acceaegeag geagmagegg gseeggteaa tgaacteeay tegtggettg gggtkgaegg
                                                                                                                                                                                                                           180
     tkaagtgcag gaagaggctg accaectege ggtecaecag gatgceegae tgtgegggae
                                                                                                                                                                                                                           240
     ctgcagcgaa actectcgat ggtcatgagc gggaagcgaa tgaggcccag ggccttgccc
                                                                                                                                                                                                                           300
     agaacettee geetgttete tggegteace tgeagetget geegetgaea eteggeeteg
                                                                                                                                                                                                                           360
     gaccagegga caaaeggert tgaaeageeg caeeteaegg atgeeeagtg tgtegegete
                                                                                                                                                                                                                           420
     caggammgsc accagegtgt ccaggtcaat gteggtgaag eceteegegg gtratggegt
                                                                                                                                                                                                                           480
     ctgcagtgtt tttgtcgatg ttctccaggc acaggctggc cagctgcggt tcatcgaaga
                                                                                                                                                                                                                           540
     gtogogootg ogtgagoago atgaaggogt tgtoggotog cagttottot toaggaacto
                                                                                                                                                                                                                           600
                                                                                                                                                                                                                           608
     cacgcaat
                       <210> 194
                       <211> 392
                       <212> DNA
                       <213> Homo sapien
                      7 (1) 1, 35, 8 1, 72 to 12 person hopewall 6 (220) 25 for 148 3 1, 100 (40 person 14 person 16 person 1
                      <221> misc_feature of Aug 10 to the man and aug
                      <222> (1).1.(392) - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 - 2.00 
                                                                                         go sympler style in roppy - oppoyer og:
                      <400> 194
    gaacggctgg accttgcctc gcattgtgct tgctggcagg gaataccttg gcaagcagyt
                                                                                                                                                                                                                              60
```

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```
ccagtccgag cagccccaga ccgctgccgc ccgaagctaa gcctgcctct ggccttcccc
                                                                        120
tccgcctcaa tgcagaacca gtagtgggag cactgtgttt agagttaaga gtgaacactg
                                                                        180
tttgatttta cttgggaatt tcctctgtta tatagctttt cccaatgcta atttccaaac
                                                                        240
aacaacaaca aaataacatg tttgcctgtt aagttgtata aaagtaggtg attctgtatt
                                                                        300
taaagaaaat attactgtta catatactgc ttgcaatttc tgtatttatt gktnctstgg
                                                                        360
aaataaatat agttattaaa ggttgtcant cc
                                                                        392
      <210> 195
      <211> 502
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(502)
      \langle 223 \rangle n = A,T,C or G
      <400> 195
ccsttkgagg ggtkaggkyc cagttyccga gtggaagaaa caggccagga gaagtgcgtg
                                                                         60
ccgagctgag gcagatgttc ccacagtgac ccccagagcc stgggstata gtytctgacc
                                                                        120
cctcncaagg aaagaccacs ttctggggac atgggctgga gggcaggacc tagaggcacc
                                                                        180
aagggaaggc cccattccgg ggstgttccc cgaggaggaa gggaagggc tctgtgtgcc
                                                                        240
ccccasgagg aagaggccct gagtcctggg atcagacacc ccttcacgtg tatccccaca
                                                                        300
caaatgcaag ctcaccaagg tcccctctca gtccccttcc stacaccctg ameggccact
                                                                        360
gscscacacc cacccagagc acgccacccg ccatggggar tgtgctcaag gartegengg
                                                                        420
gcarcgtgga catcingtcc cagaaggggg cagaatcicc aatagangga cigarcmstt
                                                                        480
gctnanaaaa aaaaanaaaa aa
                                                                        502
      <210> 196
      <211> 665
      <212> DNA
      <213> Homo sapien
            · - - · - - · ·
      <220>
      <221> misc_feature
      <222> (1)...(665)
      <223> n = A, T, C or G
ggttacttgg tttcattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc
                                                                        - 60
                                                                        120
cctctqqaaq ccttqcqcaq aqcqqacttt qtaattqttq qaqaataact qctqaatttt
                                                                        180
wagctgtttk gagttgatts gcaccactgc acccacaact tcaatatgaa aacyawttga
actwatttat tatcttgtga aaagtataac aatgaaaatt ttgttcatac tgtattkatc
                                                                        240
aagtatgatg aaaagcaawa gatatatatt cttttattat gttaaattat gattgccatt
                                                                        300
attaatcggc aaaatgtgga gtgtatgttc ttttcacagt aatatatgcc ttttgtaact
                                                                        360
tcacttggtt attttattgt aaatgartta caaaattctt aatttaagar aatggtatgt
                                                                        420
watatttatt tcattaattt ctttcctkgt ttacgtwaat tttgaaaaga wtgcatgatt
                                                                        480
tettgacaga aategatett gatgetgtgg aagtagtttg acceacatec ctatgagttt
                                                                      540
ttottagaat gtataaaggt tgtagcccat cnaacttcaa agaaaaaaat gaccacatac
                                                                      600
tttgcaatca ggctgaaatg tggcatgctn ttctaattcc aactttataa actagcaaan
                                                                        660
                        logologica englese en ekstyr i de logologica.
Per esperante en el en el
                                                                        665
aagtg
                            <210> 197
      <211> 492
      <212> DNA
      <213> Homo sapien
      <220>
```

```
<221> misc_feature
                       <222> (1) ... (492)
<223> n = A, T, C or G
                                                                       والمعاكب والحالوب الأواري
ttttnttttt tttttttgc aggaaggatt ccatttattg tggatgcatt ttcacaatat
                                                                                                                                                                                                                        120
     atgtttattg gagcgatcca ttatcagtga aaagtatcaa gtgtttataa natttttagg
     aaggcagatt cacagaacat gctngtcngc ttgcagtttt acctcgtana gatnacagag
                                                                                                                                                                                                                        180
  , aattatagto naaccagtaa acnaggaatt tacttttcaa aagattaaat ccaaactgaa 🕾
                                                                                                                                                                                                                        240
     caaaattcta ccctgaaact tactccatcc aaatattgga ataanagtca gcagtgatac
                                                                                                                                                                                                                        300
     attetettet gaactttaga ttttetagaa aaatatgtaa tagtgateag gaagagetet
                                                                                                                                                                                                                        360
     tgttcaaaag tacaacnaag caatgttccc ttaccatagg ccttaattca aactttgatc
                                                                                                                                                                                                                        420
     cattleacte ceateacggg agteaatget acetgggaca ettgtatttt gtteatnetg
                                                                                                                                                                                                                        480
     ancntggctt aa
                                                                                                                                                     Constitution of the contraction 
                                                                                                                                                                                                                        492
                                                                                                                                                        and the state of t
                       <210> 198
                       <211> 478
                       <212> DNA
                                                                                                                                                                                  18 19617
                       <213> Homo sapien property and a supply according to the carry against the
   <220>
    <221> misc_feature
    <222> (1)...(478)
    <223> n = A,T,C or G

<400> 198
tttnttttgn atttcantct gtannaanta ttttcattat gtttattana aaaatatnaa 60
tgtntccacn acaaatcatn ttacntnagt aagaggcan ctacattgta caacatagac 120
    tgtntccacn acaaatcatn ttacntnagt aagaggccan ctacattgta caacatacac
                                                                                                                                                                                                                       120
     tgagtatatt ttgaaaagga caagtttaaa gtanacncat attgccganc atancacatt 🐹
                                                                                                                                                                                                                       180
     tatacatggc ttgattgata tttagcacag canaaactga gtgagttacc agaaanaaat
                                                                                                                                                                                                                       240
    natatatgtc aatcngattt aagatacaaa acagatccta tggtacatan catcntgtag
                                                                                                                                                                                                                       300
    gagttgtggc tttatgttta ctgaaagtca atgcagttcc tgtacaaaga gatggccgta
                                                                                                                                                                                                                       360
    agcattctag tacctctact ccatggttaa gaatcgtaca cttatgttta catatgtnca
                                                                                                                                                                                                                       420
    gggtaagaat tgtgttaagt naanttatgg agaggtccan gagaaaaatt tgatncaa
                                                                                                                                                                                                                        478
                      <210> 199
                                                                                                                                                            \mathfrak{t} \in \mathbb{G}
                      <211> 482
                      <212> DNA
                      <213> Homo sapien
                    <220>
<221> misc feature
<222> (1)...(482)
<223> n = A,T,C or G
<400> 199
cttgt cctccaacaa aaccccttga tcaagtttgt ggcactgaca atcagaccta
 : 4,5 ·
   1, 3.1
   9-8
   A_{i} \mathbb{S}
<400>, 199
agtgacttgt cctccaacaa aaccccttga tcaagtttgt ggcactgaca atcagaccta
.tgctagttcc_tgtcatctat tcgctactaa atgcagactg gaggggacca aaaaggggca 120
__tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga 180
    agtgattcag tttcctctac ggatgagaga ctggctcaag aatatcctca tgcagcttta
    tgaagccnac totgaacacg otggttatot nagatgagaa noagagaaat aaagtonaga
    aaatttacct ggangaaaag aggetttngg etggggacca teccattgaa eettetetta
    anggacttta agaanaaact accacatgtn tgtngtatcc tggtgccngg ccgtttantg
                                                                                                                                                                                                                       420 '
    aachtngach neaccettht ggaatanant ettgachgen teetgaactt geteetetge
                                                                                                                                                                                                                       480
   ga
                                                                                                                                                                                 and the
                                                                                                                                                                                                                       482
                                                                                                                                                              TO COUNTY OF WORLD AND A STATE OF
                     <210> 200
```

<211> 270

```
<212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(270)
      <223> n = A, T, C or G
      <400> 200
cggccgcaag tgcaactcca gctggggccg tgcggacgaa gattctgcca gcagttggtc
                                                                          60
cgactgcgac gacggcggcg gcgacagtcg caggtgcagc, gcgggcgcct ggggtcttgc
                                                                         120
aaggetgage tgaegeegea gaggtegtgt caegteecae gaeettgaeg eegtegggga
                                                                         180
cagceggaac agageeeggt gaangeggga ggeetegggg ageeeetegg gaagggegge
                                                                         240
ccgagagata cgcaggtgca ggtggccgcc
                                                                         270
      <210> 201
      <211> 419
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (419)
      <223> n = A, T, C or G
      <400> 201
ttttttttt ttttggaatc tactgcgagc acagcaggtc agcaacaagt ttattttgca
gctagcaagg taacagggta gggcatggtt acatgttcag gtcaacttcc tttgtcgtgg
                                                                         120
ttgattggtt tgtctttatg ggggcggggt ggggtagggg aaancgaagc anaantaaca tggagtgggt gcaccctccc tgtagaacct ggttacnaaa gcttggggca gttcacctgg tctgtgaccg tcattttctt gacatcaatg ttattagaag tcaggatatc ttttagagag tccactgtnt ctggagggag attagggttt cttgccaana tccaancaaa atccacntga
                                                                         180
                                                                         240
                                                                         300
                                                                         360
aaaagttgga tgatncangt acngaatacc ganggcatan ttctcatant cggtggcca
                                                                         419
      <210> 202
      <211> 509
      <212> DNA
<213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1) ... (509)
      <223> n = A, T, C \text{ or } G
      <400> 202
60
tggcacttaa tccattttta tttcaaaatg tctacaaant ttnaatncnc cattatacng
                                                                         120
gtnattttnc aaaatctaaa nnttattcaa atntnagcca aantccttac ncaaatnnaa
                                                                         180
tacncncaaa aatcaaaaat atacntntct ttcagcaaac ttngttacat aaattaaaaa
                                                                         240
aatatatacg gctggtgttt tcaaagtaca attatcttaa cactgcaaac atntttnnaa
                                                                         300
ggaactaaaa taaaaaaaaa cactnccgca aaggttaaag ggaacaacaa attcntttta
                                                                         360
                                                                         420
caacancnnc nattataaaa atcatatctc aaatcttagg ggaatatata cttcacacng
ggatettaac ttttactnca ctttgtttat ttttttanaa ccattgtntt gggcccaaca
                                                                         480
caatggnaat necncenene tggactagt
      509
```

```
<213> Homo sapien
     <220>
     <221> misc feature
     <222> (1) . . . (583)
     <223> n = A, T, C \text{ or } G
     <400> 203
                                                                   60
ttttttttt tttttttga ccccctctt ataaaaaaca agttaccatt ttattttact
tacacatatt tattttataa ttggtattag atattcaaaa ggcagctttt aaaatcaaac
                                                                  120
taaatgqaaa ctgccttaga tacataattc ttaggaatta gcttaaaatc tgcctaaagt
                                                                  180
qaaaatcttc tctagctctt ttgactgtaa atttttgact cttgtaaaac atccaaattc
                                                                  240
                                                                  300
attitititi tettiaaaat tatetaatet tieeattiti teeetattee aagteaatti
gcttetetag ceteatttee tagetettat etaetattag taagtggett tttteetaaa
                                                                  360
agggaæaaca ggaagagana atggcacaca aaacaaacat tttatattca tatttctacc
                                                                  420
tacqttaata aaataqcatt ttqtqaaqcc agctcaaaag aaggcttaga tccttttatg
                                                                  480
tocattttag toactaaacg atatonaaag tgocagaatg caaaaggttt gtgaacattt
                                                                  540
                                                                  583
attcaaaagc taatataaga tatttcacat actcatcttt ctg
     <210> 204
     <211> 589
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc feature
     <222> (1)...(589)
                                 The second of the second
     <223> n = A,T,C or G
     <400> 204 ;
titttttttt tttttttt ttttttnctc ttctttttt ttganaatga ggatcgagtt.
tttcactctc tagatagggc atgaagaaaa ctcatcttc cagctttaaa ataacaatca
                                                                  120
aatctcttat gctatatcat attttaagtt aaactaatga gtcactggct tatcttctcc
                                                                  180
tgaaggaaat ctgttcattc ttctcattca tatagttata tcaagtacta ccttgcatat
                                                                  240
tgagaggttt ttcttctcta tttacacata tatttccatg tgaatttgta tcaaaccttt
                                                                  300
attttcatgc aaactagaaa ataatgtntt cttttgcata agagaagaga acaatatnag
                                                                  360
cattacaaaa ctgctcaaat tgtttgttaa gnttatccat tataattagt tnggcaggag
                                                                  420
ctaatacaaa tcacatttac ngacnagcaa taataaaact gaagtaccag ttaaatatcc
                                                                  480
aaaataatta aaggaacatt tttagcctgg gtataattag ctaattcact ttacaagcat
                                                                  540
ttattnagaa tgaattcaca tgttattatt ccntagccca acacaatgg
                                                                  589
     <210> 205
     <211> 545
     <212> DNA
     <213> Homo sapien
          rake kulundah langga dari kecamatan dan beratah dari
     <221> misc_feature, and server a members as a server a
     <223> n = A, T, C or Gues when the last light and white gut a
     tttttntttt ttttttcagt aataatcaga acaatattta tttttatatt taaaattcat 3000 60
agaaaagtgc cttacattta ataaaagttt gtttctcaaa gtgatcagag gaattagata........ 120
tngtcttgaa caccaatatt aatttgagga aaatacacca aaatacatta agtaaattat
ttaagatcat agagettgta agtgaaaaga taaaatttga eetcagaaac tetgageatt 🐇
                                                                  240
aaaaatccac tattagcaaa taaattacta tggacttctt gctttaattt tgtgatgaat:
                                                                  300
atggggtgtc actggtaaac caacacattc tgaaggatac attacttagt gatagattet :::-
```

```
tatgtacttt gctanatnac gtggatatga gttgacaagt ttctctttct tcaatctttt
                                                                                                                                                                                                                              420
aaggggcnga ngaaatgagg aagaaaagaa aaggattacg catactgttc tttctatngg
                                                                                                                                                                                                                              480
aaggattaga tatgtttcct ttgccaatat taaaaaaata ataatgttta ctactagtga
                                                                                                                                                                                                                              540
                                                                                                                                                                                                                              545
aaccc
                   <210> 206
                   <211> 487
                   <212> DNA
                   <213> Homo sapien
                   <220>
                   <221> misc feature
                   <222>. (1) ... (487)
                   <223> n = A, T, C or G
                   <400> 206
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                                                                                                                                                                                                                                 60
catttattag ctctgcaact tacatattta aattaaagaa acgttnttag acaactgtna
                                                                                                                                                                                                                               120
caatttataa atgtaaggtg ccattattga gtanatatat tcctccaaga gtggatgtgt
                                                                                                                                                                                                                              180
cccttctccc accaactaat gaancagcaa cattagttta attttattag tagatnatac
                                                                                                                                                                                                                               240
                                                                                                                                                                                                                               300
 actgctgcaa acgctaattc tcttctccat ccccatgtng atattgtgta tatgtgtgag
ttggtnagaa tgcatcanca atctnacaat caacagcaag atgaagctag gcntgggctt
                                                                                                                                                                                                                               360
tcggtgaaaa tagactgtgt ctgtctgaat caaatgatct gacctatcct cggtggcaag
                                                                                                                                                                                                                               420
 aactettega accepttect caaaggenge tecacattt gtggentetn ttgeacttet
                                                                                                                                                                                                                               480
                                                                                                                                                                                                                               487
 ttcaaaa
                    <210> 207
                    <211> 332
                    <212> DNA
                    <213> Homo sapien
                    <220>
                    <221> misc feature
                    <222> (1)...(332)
                    <223> n = A, T, C or G
 tgaattggct aaaagactgc atttttanaa ctagcaactc ttatttcttt cctttaaaaa
                                                                                                                                                                                                                                  60
 tacatagcat taaatcccaa atcctattta aagacctgac agcttgagaa ggtcactact
                                                                                                                                                                                                                               120
 gcatttatag gaccttctgg tggttctgct gttacntttg aantctgaca atccttgana
                                                                                                                                                                                                                                180
 atctttgcat gcagaggagg taaaaggtat tggattttca cagaggaana acacagcgca
                                                                                                                                                                                                                                240
 gaaatgaagg ggccaggctt actgagcttg tccactggag ggctcatggg tgggacatgg
                                                                                                                                                                                                                                300
                                                                                                                                                                                                                                332
 aaaagaaggc agcctaggcc ctggggagcc ca
                     <210> 208
                                                                                  (i) Sign of the graph of the graph of the argument of the argument of the argument of the graph of the gra
                    <211> 524
                     <212> DNA
                     <213> Homo sapien
                                                                                                              Contract to the part of the contract of the state of the contract of the contr
                     <220>
                     <221> misc feature
                     <222> (1)...(524)
                     <223> n = A, T, C \text{ or } G
                    <400> 208
 agggcgtggt gcggagggcg ttactgtttt gtctcagtaa caataaatac aaaaagactg
                                                                                                                                                                                                                                   60
 gttgtgttcc ggccccatcc aaccacgaag ttgatttctc ttgtgtgcag agtgactgat
                                                                                                                                                                                                                                120
 tttaaaggac atggagcttg tcacaatgtc acaatgtcac agtgtgaagg gcacactcac
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|                                                                    |                                                                                                                                                                             | ttcacattta                                                                                                                                                            |                                                                                             |                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                | 240                                                        |
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|                                                                    |                                                                                                                                                                             |                                                                                                                                                                       | aacttgcaga                                                                                  |                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                | 300<br>360                                                 |
|                                                                    |                                                                                                                                                                             |                                                                                                                                                                       | atattaatta<br>caaactaagc                                                                    |                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                | 420                                                        |
|                                                                    |                                                                                                                                                                             |                                                                                                                                                                       | tcaccttgac                                                                                  |                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                | 480                                                        |
|                                                                    |                                                                                                                                                                             |                                                                                                                                                                       | tccggtaatg                                                                                  |                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 45 %                                                                                                           | 524                                                        |
|                                                                    |                                                                                                                                                                             | ,                                                                                                                                                                     | 33 3                                                                                        | <b>-</b>                                                                                                                                                                                                                         | -                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                | ξ.                                                         |
|                                                                    |                                                                                                                                                                             | > 209                                                                                                                                                                 |                                                                                             |                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | `n ;                                                                                                           | -                                                          |
|                                                                    |                                                                                                                                                                             | > 159                                                                                                                                                                 |                                                                                             |                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                |                                                            |
|                                                                    |                                                                                                                                                                             | > DNA                                                                                                                                                                 |                                                                                             | · '                                                                                                                                                                                                                              | : i                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 4                                                                                                              |                                                            |
|                                                                    | <2132                                                                                                                                                                       | > Homo sapie                                                                                                                                                          | 311                                                                                         | •                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 4 4 4 4 4                                                                                                      |                                                            |
|                                                                    | <4002                                                                                                                                                                       | > 209                                                                                                                                                                 | 1                                                                                           |                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 1. 1. 1. 4. 1.7                                                                                                | *                                                          |
| gggtga                                                             |                                                                                                                                                                             |                                                                                                                                                                       | gccatggaga                                                                                  | aaattccagt                                                                                                                                                                                                                       | gtcagcattc                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | ttgctccttg                                                                                                     | 60                                                         |
| tggcc                                                              | ctctc                                                                                                                                                                       | ctacactctg                                                                                                                                                            | gccagagata                                                                                  | ccacagtcaa                                                                                                                                                                                                                       | acctggagcc                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | aaaaaggaca                                                                                                     | 120                                                        |
| caaag                                                              | gactc                                                                                                                                                                       | tcgacccaaa                                                                                                                                                            | ctgccccaga                                                                                  | ccctctcca                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                | 159                                                        |
| •                                                                  | -050                                                                                                                                                                        |                                                                                                                                                                       | ្រំ ) ប្រាការ<br>ព្រះប្រាក្ស                                                                | Mitalia (Mila)<br>La calenda (Calenda)                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | ಜ್ಞಾನ ಬೆಂದು ಬಟ್ಟಿ ಎಂದು<br>ಎಂದು ಬರುಗಳು ಅಂದರುವು                                                                  | ing a set for a                                            |
| •                                                                  | <2102                                                                                                                                                                       | > 210                                                                                                                                                                 | egenerativsky statement.<br>Budietis et ble bit i gest                                      | ji maga katan kalangan salah sal<br>Salah salah sa | and a second of the second of |                                                                                                                | erana arangan<br>Manggarangan                              |
|                                                                    | <21:25                                                                                                                                                                      | > DNIA de di Sa                                                                                                                                                       | 15 1 t t                                                                                    | J. 75 1. 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1                                                                                                                                                                                     | Bar Maria 2 - A.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Salah Sa | trada Ligar                                                |
| f                                                                  | <2133                                                                                                                                                                       | Homo sanie                                                                                                                                                            | en .                                                                                        | 5.750000                                                                                                                                                                                                                         | Light Mary Control                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 13 44,1 30                                                                                                     |                                                            |
| 200                                                                |                                                                                                                                                                             | 11 11 12 12 10 -                                                                                                                                                      | المتروا فأنبي فياليوس                                                                       | 75 J. 24                                                                                                                                                                                                                         | 50、46、沙瓦 35年                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | er day a                                                                                                       | <b>7.</b> St. 2., 1                                        |
| 1 2 25                                                             | <220                                                                                                                                                                        | <b>&gt;</b> 00 ⊈ . 04 04 (3) (                                                                                                                                        |                                                                                             | in the sile tw                                                                                                                                                                                                                   | F .727                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | in a regard of the                                                                                             | 5 4 11 A 4 T C                                             |
| 43.8%                                                              | <221                                                                                                                                                                        | <pre>&gt; misc_feat:</pre>                                                                                                                                            | ire                                                                                         |                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 2012                                                                                                           |                                                            |
| , ; '                                                              |                                                                                                                                                                             | (1)(256                                                                                                                                                               |                                                                                             |                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                |                                                            |
|                                                                    | <2232                                                                                                                                                                       | n = A, T, C                                                                                                                                                           | or G                                                                                        |                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                | ) b                                                        |
|                                                                    | <400>                                                                                                                                                                       | > 210                                                                                                                                                                 |                                                                                             |                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 404 471                                                                                                        | 6                                                          |
| acted                                                              |                                                                                                                                                                             |                                                                                                                                                                       | agaggagaga                                                                                  | gctctgttag                                                                                                                                                                                                                       | ttctatatta                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | ttgaactgcc                                                                                                     | 60                                                         |
| ~~~~                                                               |                                                                                                                                                                             |                                                                                                                                                                       |                                                                                             |                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                |                                                            |
| actgaa                                                             | atttc                                                                                                                                                                       | tttccacttg                                                                                                                                                            | gactattaca                                                                                  | tgccanttga                                                                                                                                                                                                                       | gggactaatg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | gaaaaacgta                                                                                                     | 120                                                        |
| actgaa<br>tgggga                                                   | atttc<br>agatt                                                                                                                                                              | tttccacttg<br>ttanccaatt                                                                                                                                              | gactattaca<br>tangtntgta                                                                    | tgccanttga<br>aatggggaga                                                                                                                                                                                                         | gggactaatg<br>ctggggcagg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | gaaaaacgta<br>cgggagagat                                                                                       | 120<br>180                                                 |
| actgaa<br>tgggga<br>ttgcag                                         | atttc<br>agatt<br>gggtg                                                                                                                                                     | tttccacttg<br>ttanccaatt<br>naaatgggan                                                                                                                                | gactattaca                                                                                  | tgccanttga<br>aatggggaga                                                                                                                                                                                                         | gggactaatg<br>ctggggcagg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | gaaaaacgta<br>cgggagagat                                                                                       | 120<br>180<br>240                                          |
| actgaa<br>tgggga<br>ttgcag                                         | atttc<br>agatt<br>gggtg                                                                                                                                                     | tttccacttg<br>ttanccaatt                                                                                                                                              | gactattaca<br>tangtntgta                                                                    | tgccanttga<br>aatggggaga                                                                                                                                                                                                         | gggactaatg<br>ctggggcagg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | gaaaaacgta<br>cgggagagat                                                                                       | 120<br>180                                                 |
| actgaa<br>tgggga<br>ttgcag                                         | atttc<br>agatt<br>gggtg<br>atgct                                                                                                                                            | tttccacttg<br>ttanccaatt<br>naaatgggan<br>aaatca                                                                                                                      | gactattaca<br>tangtntgta                                                                    | tgccanttga<br>aatggggaga                                                                                                                                                                                                         | gggactaatg<br>ctggggcagg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | gaaaaacgta<br>cgggagagat                                                                                       | 120<br>180<br>240                                          |
| actgaa<br>tgggga<br>ttgcag                                         | atttc<br>agatt<br>gggtg<br>atgct<br><210>                                                                                                                                   | tttccacttg<br>ttanccaatt<br>naaatgggan                                                                                                                                | gactattaca<br>tangtntgta                                                                    | tgccanttga<br>aatggggaga                                                                                                                                                                                                         | gggactaatg<br>ctggggcagg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | gaaaaacgta<br>cgggagagat                                                                                       | 120<br>180<br>240                                          |
| actgaa<br>tgggga<br>ttgcag                                         | atttc<br>agatt<br>gggtg<br>atgct<br><210><br><211>                                                                                                                          | tttccacttg ttanccaatt naaatgggan aaatca > 211 > 264 > DNA                                                                                                             | gactattaca<br>tangtntgta<br>ggctggtttg                                                      | tgccanttga<br>aatggggaga<br>ttanatgaac                                                                                                                                                                                           | gggactaatg<br>ctggggcagg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | gaaaaacgta<br>cgggagagat                                                                                       | 120<br>180<br>240                                          |
| actgaa<br>tgggga<br>ttgcag                                         | atttc<br>agatt<br>gggtg<br>atgct<br><210><br><211><br><212>                                                                                                                 | tttccacttg ttanccaatt naaatgggan aaatca > 211 > 264 > DNA > Homo sapie                                                                                                | gactattaca<br>tangtntgta<br>ggctggtttg                                                      | tgccanttga<br>aatggggaga<br>ttanatgaac                                                                                                                                                                                           | gggactaatg<br>ctggggcagg<br>agggacatag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | gaaaaacgta<br>cgggagagat<br>gaggtaggca                                                                         | 120<br>180<br>240<br>256                                   |
| actgaa<br>tgggga<br>ttgcag                                         | atttc<br>agatt<br>gggtg<br>atgct<br><210><br><211><br><212><br><213>                                                                                                        | tttccacttg ttanccaatt naaatgggan aaatca  211 264 DNA Homo saple                                                                                                       | gactattaca<br>tangtntgta<br>ggctggtttg                                                      | tgccanttga<br>aatggggaga<br>ttanatgaac                                                                                                                                                                                           | gggactaatg<br>ctggggcagg<br>agggacatag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | gaaaaacgta<br>cgggagagat                                                                                       | 120<br>180<br>240<br>256                                   |
| actgaa<br>tgggga<br>ttgcag<br>ccagga                               | atttc<br>agatt<br>gggtg<br>atgct<br><210><br><211><br><212><br><213>                                                                                                        | tttccacttg ttanccaatt naaatgggan aaatca  211 264 DNA Homo saple                                                                                                       | gactattaca<br>tangtntgta<br>ggctggtttg                                                      | tgccanttga<br>aatggggaga<br>ttanatgaac                                                                                                                                                                                           | gggactaatg<br>ctggggcagg<br>agggacatag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | gaaaaacgta<br>cgggagagat<br>gaggtaggca                                                                         | 120<br>180<br>240<br>256                                   |
| actgaa<br>tgggga<br>ttgcag<br>ccagga                               | atttc<br>agatt<br>yggtg<br>atgct<br><210><br><211><br><212><br><213><br><220>                                                                                               | tttccacttg ttanccaatt naaatgggan aaatca  211 264 DNA Homo sapie                                                                                                       | gactattaca<br>tangtntgta<br>ggctggtttg                                                      | tgccanttga<br>aatggggaga<br>ttanatgaac                                                                                                                                                                                           | gggactaatg<br>ctggggcagg<br>agggacatag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | gaaaaacgta<br>cgggagagat<br>gaggtaggca                                                                         | 120<br>180<br>240<br>256                                   |
| actgaa<br>tgggga<br>ttgcag<br>ccagga                               | atttc<br>agatt<br>gggtg<br>atgct<br><210><br><211><br><212><br><213><br><220><br><221>                                                                                      | tttccacttg ttanccaatt naaatgggan aaatca  211 264 DNA Homo sapie misc_featu (1) (264                                                                                   | gactattaca<br>tangtntgta<br>ggctggtttg                                                      | tgccanttga aatggggaga ttanatgaac                                                                                                                                                                                                 | gggactaatg<br>ctggggcagg<br>agggacatag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | gaaaaacgta<br>cgggagagat<br>gaggtaggca                                                                         | 120<br>180<br>240<br>256                                   |
| actgaa<br>tgggga<br>ttgcag<br>ccagga                               | atttc<br>agatt<br>yggtg<br>atget<br><210><br><211><br><212><br><220><br><221><br><222><br><223>                                                                             | tttccacttg ttanccaatt naaatgggan aaatca  211 264 DNA Homo saple misc_featu (1)(264 n = A,T,C                                                                          | gactattaca tangtntgta ggctggtttg  an                                                        | tgccanttga aatggggaga ttanatgaac                                                                                                                                                                                                 | gggactaatg<br>ctggggcagg<br>agggacatag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | gaaaaacgta<br>cgggagagat<br>gaggtaggca                                                                         | 120<br>180<br>240<br>256                                   |
| actgaa<br>tgggga<br>ttgcag<br>ccagga                               | atttc<br>agatt<br>yggtg<br>atget<br><210><br><211><br><212><br><2213><br><220><br><222><br><222><br><223>                                                                   | tttccacttg ttanccaatt naaatgggan aaatca  211 264 DNA Homo saple  misc_featu (1) (264 n = A,T,C                                                                        | gactattaca tangtntgta ggctggtttg  en ire i)                                                 | tgccanttga aatggggaga ttanatgaac                                                                                                                                                                                                 | gggactaatg<br>ctggggcagg<br>agggacatag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | gaaaaacgta<br>cgggagagat<br>gaggtaggca                                                                         | 120<br>180<br>240<br>256                                   |
| actgaa<br>tgggga<br>ttgcag<br>ccagga                               | atttc<br>agatt<br>yggtg<br>atget<br><210><br><211><br><212><br><223><br><222><br><223><br><400><br>ytttt                                                                    | tttccacttg ttanccaatt naaatgggan aaatca  211 264 DNA Homo saple (1)(264 n = A,T,C                                                                                     | gactattaca tangtntgta ggctggtttg  an  are  are agcattgaga                                   | tgccanttga aatggggaga ttanatgaac                                                                                                                                                                                                 | gggactaatg<br>ctggggcagg<br>agggacatag<br>taacgtgaca                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | gaaaaacgta<br>cgggagagat<br>gaggtaggca                                                                         | 120<br>180<br>240<br>256                                   |
| actgaa<br>tgggga<br>ttgcag<br>ccagga                               | atttc agatt ggtg atget <210> <211> <212> <213> <220> <221> <222> <223> <400> gtttt agac agac agac agac agac agac aga                                                        | tttccacttg ttanccaatt naaatgggan aaatca  211 264 DNA Homo saple (1)(264 n = A,T,C                                                                                     | gactattaca tangtntgta ggctggtttg  an  are  agcattgaga ctttgttctg                            | tgccanttga aatggggaga ttanatgaac  gagctctcct agggataatt                                                                                                                                                                          | gggactaatg<br>ctggggcagg<br>agggacatag<br>taacgtgaca<br>ttctgataaa                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | gaaaaacgta<br>cgggagagat<br>gaggtaggca<br>caatggaagg<br>qtcttqctqt                                             | 120<br>180<br>240<br>256                                   |
| actgas<br>tggggs<br>ttgcas<br>ccaggs<br>acatts<br>actggs<br>atatts | atttc<br>agatt<br>gggtg<br>atgct<br><210><br><211><br><212><br><221><br><220><br><221><br><222><br><400><br>gtttt<br>acac                                                   | tttccacttg ttanccaatt naaatgggan aaatca  211 264 DNA Homo sapid (1)(264 n = A,T,C  211 tttgagataa atacccacat acatatgtta                                               | gactattaca tangtntgta ggctggtttg  an  are  agcattgaga cttgttctg tatattattc                  | tgccanttga aatggggaga ttanatgaac  gagctctcct agggataatt agttccatgt                                                                                                                                                               | gggactaatg<br>ctggggcagg<br>agggacatag<br>taacgtgaca<br>ttctgataaa<br>ttatagccta                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | gaaaaacgta<br>cgggagagat<br>gaggtaggca<br>caatggaagg<br>gtcttgctgt<br>gttaaggaga                               | 120<br>180<br>240<br>256                                   |
| actgas<br>tggggs<br>ttgcas<br>ccaggs<br>actggs<br>atatts<br>ggggas | atttc<br>agatt<br>gggtg<br>atgct<br><210><br><211><br><212><br><221><br><220><br><221><br><222><br><400><br>gtttt<br>acac<br>aagc<br>gatac                                  | tttccacttg ttanccaatt naaatgggan aaatca  211 264 DNA Homo sapid (1)(264 n = A,T,C  211 tttgagataa atacccacat acatatgtta                                               | gactattaca tangtntgta ggctggtttg  an  are  agcattgaga ctttgttctg tatattattc aggactgaaa      | tgccanttga aatggggaga ttanatgaac  gagctctcct agggataatt agttccatgt                                                                                                                                                               | gggactaatg<br>ctggggcagg<br>agggacatag<br>taacgtgaca<br>ttctgataaa<br>ttatagccta<br>agtnggaaaa                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | gaaaaacgta<br>cgggagagat<br>gaggtaggca<br>caatggaagg<br>gtcttgctgt<br>gttaaggaga<br>cagaaaaaga                 | 120<br>180<br>240<br>256<br>60<br>120<br>180<br>240<br>264 |
| actgas<br>tggggs<br>ttgcas<br>ccaggs<br>actggs<br>atatts<br>ggggas | atttc<br>agatt<br>gggtg<br>atgct<br><210><br><211><br><2212><br><2213><br><222><br><222><br><400><br>gtttt<br>acac<br>aagc<br>gatac                                         | tttccacttg ttanccaatt naaatgggan aaatca  211 264 DNA Homo sapid (1) (264 n = A,T,C  211 tttgagataa atacccacat acatatgtta attcngaaag caaatgagaa                        | gactattaca tangtntgta ggctggtttg  an  are  agcattgaga ctttgttctg tatattattc aggactgaaa      | tgccanttga aatggggaga ttanatgaac  gagctctcct agggataatt agttccatgt                                                                                                                                                               | gggactaatg<br>ctggggcagg<br>agggacatag<br>taacgtgaca<br>ttctgataaa<br>ttatagccta<br>agtnggaaaa                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | gaaaaacgta<br>cgggagagat<br>gaggtaggca<br>caatggaagg<br>gtcttgctgt<br>gttaaggaga<br>cagaaaaaga                 | 120<br>180<br>240<br>256<br>60<br>120<br>180<br>240<br>264 |
| actgas<br>tggggs<br>ttgcas<br>ccaggs<br>actggs<br>atatts<br>ggggas | atttc<br>agatt<br>gggtg<br>atgct<br><210><br><211><br><2212><br><2213><br><222><br><222><br><400><br>gtttt<br>acac<br>aagc<br>gatac<br><210>                                | tttccacttg ttanccaatt naaatgggan aaatca  211 264 DNA Homo sapie (1) (264 n = A,T,C  211 tttgagataa atacccacat acatatgtta attcngaaag caaatgagaa                        | gactattaca tangtntgta ggctggtttg  an  are  agcattgaga ctttgttctg tatattattc aggactgaaa      | tgccanttga aatggggaga ttanatgaac  gagctctcct agggataatt agttccatgt                                                                                                                                                               | gggactaatg<br>ctggggcagg<br>agggacatag<br>taacgtgaca<br>ttctgataaa<br>ttatagccta<br>agtnggaaaa                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | gaaaaacgta<br>cgggagagat<br>gaggtaggca<br>caatggaagg<br>gtcttgctgt<br>gttaaggaga<br>cagaaaaaga                 | 120<br>180<br>240<br>256<br>60<br>120<br>180<br>240<br>264 |
| actgas<br>tggggs<br>ttgcas<br>ccaggs<br>actggs<br>atatts<br>ggggas | <pre>atttc agatt gggtg atgct &lt;210&gt; &lt;211&gt; &lt;2212&gt; &lt;2213&gt; &lt;222&gt; &lt;222&gt; &lt;400&gt; gttt acac aagc gatac aggag &lt;210&gt; &lt;211&gt;</pre> | tttccacttg ttanccaatt naaatgggan aaatca  211 264 DNA Homo sapid (1) (264 n = A,T,C  211 tttgagataa ataccacat acatatgtta attcngaaag caaatgagaa  212 328                | gactattaca tangtntgta ggctggtttg  an  are  agcattgaga ctttgttctg tatattattc aggactgaaa      | tgccanttga aatggggaga ttanatgaac  gagctctcct agggataatt agttccatgt                                                                                                                                                               | gggactaatg<br>ctggggcagg<br>agggacatag<br>taacgtgaca<br>ttctgataaa<br>ttatagccta<br>agtnggaaaa                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | gaaaaacgta<br>cgggagagat<br>gaggtaggca<br>caatggaagg<br>gtcttgctgt<br>gttaaggaga<br>cagaaaaaga                 | 120<br>180<br>240<br>256<br>60<br>120<br>180<br>240<br>264 |
| actgas<br>tggggs<br>ttgcas<br>ccaggs<br>actggs<br>atatts<br>ggggas | **************************************                                                                                                                                      | tttccacttg ttanccaatt naaatgggan aaatca  211 264 DNA Homo sapid (1) (264 n = A,T,C  211 tttgagataa atacccacat acatatgtta attcngaaag caaatgagaa  212 328 DNA           | gactattaca tangtntgta ggctggtttg  an  are  agcattgaga ctttgttctg tatattattc aggactgaaa gcct | tgccanttga aatggggaga ttanatgaac  gagctctcct agggataatt agttccatgt                                                                                                                                                               | gggactaatg<br>ctggggcagg<br>agggacatag<br>taacgtgaca<br>ttctgataaa<br>ttatagccta<br>agtnggaaaa                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | gaaaaacgta<br>cgggagagat<br>gaggtaggca<br>caatggaagg<br>gtcttgctgt<br>gttaaggaga<br>cagaaaaaga                 | 120<br>180<br>240<br>256<br>60<br>120<br>180<br>240<br>264 |
| actgas<br>tggggs<br>ttgcas<br>ccaggs<br>actggs<br>atatts<br>ggggas | **************************************                                                                                                                                      | tttccacttg ttanccaatt naaatgggan aaatca  211 264 DNA Homo sapie (1)(264 n = A,T,C  211 tttgagataa atacccacat acatatgtta attcngaaag caaatgagaa  212 328 DNA Homo sapie | gactattaca tangtntgta ggctggtttg  an  are  agcattgaga ctttgttctg tatattattc aggactgaaa gcct | tgccanttga aatggggaga ttanatgaac  gagctctcct agggataatt agttccatgt gaaatactca                                                                                                                                                    | gggactaatg<br>ctggggcagg<br>agggacatag<br>taacgtgaca<br>ttctgataaa<br>ttatagccta<br>agtnggaaaa                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | gaaaaacgta<br>cgggagagat<br>gaggtaggca<br>caatggaagg<br>gtcttgctgt<br>gttaaggaga<br>cagaaaaaga                 | 120<br>180<br>240<br>256<br>60<br>120<br>180<br>240<br>264 |
| actgas<br>tggggs<br>ttgcas<br>ccaggs<br>actggs<br>atatts<br>ggggas | **************************************                                                                                                                                      | tttccacttg ttanccaatt naaatgggan aaatca  211 264 DNA Homo sapie (1)(264 n = A,T,C  211 tttgagataa atacccacat acatatgtta attcngaaag caaatgagaa  212 328 DNA Homo sapie | gactattaca tangtntgta ggctggtttg  an  are  agcattgaga ctttgttctg tatattattc aggactgaaa gcct | tgccanttga aatggggaga ttanatgaac  tanatgaac  gagctctcct agggataatt agttccatgt gaaatactca                                                                                                                                         | gggactaatg<br>ctggggcagg<br>agggacatag<br>taacgtgaca<br>ttctgataaa<br>ttatagccta<br>agtnggaaaa                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | gaaaacgta<br>cgggagagat<br>gaggtaggca<br>caatggaagg<br>gtcttgctgt<br>gttaaggaga<br>cagaaaaaga                  | 120<br>180<br>240<br>256<br>60<br>120<br>180<br>240<br>264 |

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<222> (1)...(328)
      <223> n = A,T,C or G
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ggatttaatg ttgtctcagc ttgggcactt cagttaggac ctaaggatgc cagccggcag
                                                                       120
otttatatat gcagcaacaa tattcaagcg cgacaacagg ttattgaact tgcccgccag
                                                                       180
                                                                       240
ttnaatttca ttcccattga cttgggatcc ttatcatcag ccagagagat tgaaaattta
cccctacnac tetttactet etgganaggg ccagtggtgg tagetataag ettggecaca
                                                                       300
                                                                       328
ttttttttc ctttattcct ttgtcaga
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      <211> 250
      ≤212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
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                                                                         60
taaagcattg ctcactgaag ggatagaagt gactgccagg agggaaagta agccaaggct
                                                                       120
cattatgcca aagganatat acatttcaat totocaaact tottoctcat tocaagagtt
                                                                       180
                                                                       240
ttcaatattt gcatgaacct gctgataanc catgttaana aacaaatatc tctctnacct
                                                                       250
tctcatcggt
      <210> 214
      <211> 444
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(444)
      <223> n = A, T, C or G
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                                                                         60
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gatttaatgt tgtctcagct tgggcacttc agttaggacc taaggatgcc agccggcagg
                                                                       180
tttatatatg cagcaacaat attcaagcgc gacaacaggt tattgaactt gcccgccagt
tgaatttcat tcccattgac ttgggatcct tatcatcagc canagagatt gaaaatttac
                                                                       240
ccctacgact ctttactctc tggagagggc cagtggtggt agctataagc ttggccacat
                                                                       300
tttttttcc tttattcctt tgtcagagat gcgattcatc catatgctan aaaccaacag
                                                                       360
agtgactttt acaaaattcc tataganatt gtgaataaaa ccttacctat agttgccatt
                                                                        420
actttqctct ccctaatata cctc
      <210> 215
      <211> 366
      <212> DNA
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      <220>
      <221> misc_feature
      <222> (1)...(366)
      <223> n = A, T, C or G
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                                                                    120
 cattatgcca aagganatat acatttcaat tctccaaact tcttcctcat tccaagagtt
                                                                   180
ttcaatattt gcatgaacct gctgataagc catgttgaga aacaaatatc tctctgacct
                                                                   240
tctcatcggt aagcagaggc tgtaggcaac atggaccata gcgaanaaaa aacttagtaa
                                                                   300
tccaagctgt tttctacact gtaaccaggt ttccaaccaa ggtggaaatc tcctatactt
                                                                   360
                                                                    366
ggtgcc
                     EST SERVICE SERVICES
      <210> 216
      <211> 260
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(260)
      <223> n = A, T, C or G
    <400> 216
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                                                                    60
 caagacaggg gcctaaggag ggtctccaca ctgctnntaa gggctnttnc attttttat
                                                                   120
taataaaaag tnnaaaaggc ctcttctcaa ctttttccc ttnggctgga aaatttaaaa
                                                                   180
 atcaaaaatt teetnaagtt nteaagetat eatatatat intateetgaa aaageaacat
                                                                   240
aattetteet teeeteett
                                                                   260
                     កាស់ ស្រុស ក្រុងទេស សុខ
      <210> 217
      <211> 262
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(262)
      <223> n = A, T, C or G
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                                                                    60
tcttqcctat aattttctat tttaataaqq aaataqcaaa ttqqqqtqqq qqqaatqtaq
                                                                   120
                                                                   180
ggcattctac agtttgagca aaatgcaatt aaatgtggaa ggacagcact gaaaaatttt
atgaataate totatgatta tatoteeta gagtagattt ataattagee aettaceeta
                                                                   240
atatccttca tgcttgtaaa gt
                                                                   262
      <210> 218 (**) (**) (**) (**)
      <211> 205
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(205)
      <223> n = A, T, C or G
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                                                                    60
                                                                   120
cccctatcaa ctcccttttg tagtaaactt ggaaccttgg aaatgaccag gccaagactc
aggectecce agttetactg acctttgtcc ttangtntna ngtecagggt tgctaggaaa
                                                                   180
anaaatcagc agacacaggt gtaaa
                                                                   205
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     <211> 114
     <212> DNA
      <213> Homo sapien
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accacgaagt tgatttctct tgtgtgcaga gtgactgatt ttaaaggaca tgga
     <210> 220
      <211> 93
      <212> DNA 1 . .
     <213> Homo sapien
     <400> 220
actagocago acaaaaggca gggtagoctg aattgctttc tgctctttac atttctttta
aaataagcat ttagtgetca gteeetactg agt
                                                                   93
                <210> 221
     <211> 167
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc_feature
     <222> (1) ... (167)
     <223> n = A, T, C or G
     <400> 221
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tcttttgccc agcctgtggc tctactgtag taagtttctg ctgatgagga gccagnatgc
                                                                  120
cccccactac ettecctgac getecccana aatcacccaa cetetgt
     <210> 222
     <211> 351
     <212> DNA
     <213> Homo sapien
     <400> 222
agggegtggt geggagggeg gtactgacet cattagtagg aggatgcatt ctggcacecc 60
gttetteace tgteececaa teettaaaag gecatactge ataaagteaa caacagataa 120
atgtttgctg aattaaagga tggatgaaaa aaattaataa tgaatttttg cataatccaa 180 ttttctcttt tatatttcta gaagaagttt ctttgagcct attagatccc gggaatcttt 240
taggtgagca tgattagaga gcttgtaggt tgcttttaca tatatctggc atatttgagt 300
ctcgtatcaa aacaatagat tggtaaaggt ggtattattg tattgataag t 351
                                   again an agréag é in Éireannach i gir na heart agus t
     <210> 223
     <211> 383
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc_feature
     <222> (1) ... (383)
     <223> n = A, T, C or G
     <400> 223
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| aaaacaaaca aacaaaaaaa acaattette at<br>tggtaattat ggtcaattta atwrtrttkt gg<br>ttaaaatgte tgtgccaaaa ttttgtattt ta<br>tgccaaagga agtctaagga attagtagtg to<br>taaaagattt tgattteetg gaatgacaat ta<br>ataggaccac agtctteact tetgataett gd<br>accattaage tatatgttta aaa | gggcatttc c<br>atttggaga c<br>tcccmtcac t<br>atattttaa c | ettacattgt<br>ettcttatca<br>etgtttggag<br>etttggtggg | cttgacaaga<br>aaagtaatgc<br>tgtgctattc<br>ggaaanagtt | 60<br>120<br>180<br>240<br>300<br>360<br>383 |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------|------------------------------------------------------|------------------------------------------------------|----------------------------------------------|
| <210> 224<br><211> 320<br><212> DNA<br><213> Homo sapien                                                                                                                                                                                                            |                                                          | e e                                                  |                                                      |                                              |
| <400> 224 cccctgaagg cttcttgtta gaaaatagta caaaagtttgt gacattgtag tagggagtgt gt ggatacatgg ttaaaggata raagggcaat at                                                                                                                                                 | tacccctta c<br>ttttatcat a                               | tccccatca<br>tgttctaaa                               | aaaaaaaaat<br>agagaaggaa                             | 60<br>120<br>∃180                            |
| gagaaaatac tactttctcr aaatggaagc co<br>aaatgtggcc gtccatcctc ctttaragtt go<br>tttaractcm gcattgtgac                                                                                                                                                                 | cttaaaggt g<br>catgacttg g                               | ctttgatac<br>acacggtaa                               | tgaaggacac<br>ctgttgcagt                             | 240<br>300<br>320                            |
| <210> 225<br><211> 1214<br><212> DNA<br><213> Homo sapien                                                                                                                                                                                                           |                                                          |                                                      |                                                      | -                                            |
|                                                                                                                                                                                                                                                                     |                                                          | 12.5                                                 |                                                      |                                              |
| <400> 225                                                                                                                                                                                                                                                           |                                                          |                                                      |                                                      | -                                            |
| gaggactgca gcccgcactc gcagccctgg cattctgctcgg gcgtcctggt gcatccgcag tg                                                                                                                                                                                              | aggeggeae c                                              | ggccacgga                                            | aaacgaattg<br>ctatttacaa                             | 60<br>120                                    |
| aactectaca ccateggget gggeetgeac ag                                                                                                                                                                                                                                 | gtettgagg e                                              | cgaccaaga                                            | accadddadd -                                         | 180                                          |
| cagatggtgg aggccagcct ctccgtacgg ca                                                                                                                                                                                                                                 | acccagagt a                                              | caacagacc                                            | cttactcact                                           | 240                                          |
| aacgacctca tgctcatcaa gttggacgaa to                                                                                                                                                                                                                                 | ccgtgtccg a                                              | gtctgacac                                            | catccggage                                           | 300                                          |
| atcagcattg cttcgcagtg ccctaccgcg gg                                                                                                                                                                                                                                 | ggaactett ge                                             | cctcgtttc                                            | tggctggggt                                           | 360                                          |
| ctgctggcga acggcagaat gcctaccgtg ct                                                                                                                                                                                                                                 | gcagtgcg to                                              | gaacgtgtc                                            | ggtggtgtct                                           | 420                                          |
| gaggaggtet geagtaaget etatgaeeeg et                                                                                                                                                                                                                                 | gtaccacc co                                              | cagcatgtt                                            | ctgcgccggc                                           | 480                                          |
| ggagggcaag accagaagga ctcctgcaac gg                                                                                                                                                                                                                                 | stgactctg g                                              | ggggcccct                                            | gatctgcaac                                           | 540                                          |
| gggtacttgc agggccttgt gtctttcgga aa                                                                                                                                                                                                                                 | agccccgt g                                               | tggccaagt                                            | tggcgtgcca                                           | 600                                          |
| ggtgtctaca ccaacctctg caaattcact ga<br>taactctggg gactgggaac ccatgaaatt ga                                                                                                                                                                                          | agtggatag ag                                             | gaaaaccgt                                            | ccaggccagt                                           | 660                                          |
| caggaatate tgtteceage ecetectee te                                                                                                                                                                                                                                  | raggeceag g                                              | acareerge                                            | ggaaggaatt                                           | 720<br>780                                   |
| tectectea accaagggt acagatecee ag                                                                                                                                                                                                                                   | receteét e                                               | cctcadacc                                            | caggagteca                                           | 840                                          |
| gacccccag ccctcctcc ctcagaccca gg                                                                                                                                                                                                                                   | agtccagc co                                              | cctcctccc                                            | tcagacccag                                           | 900                                          |
| gagtecagae cececagece etectecete ag                                                                                                                                                                                                                                 | racccaggg gl                                             | tecaggeee                                            | ccaacccctc                                           | 960                                          |
| ctecctcaga ctcagaggtc caagccccca ac                                                                                                                                                                                                                                 | ecctcctt co                                              | cccagaccc                                            | agaggtccag                                           | 1020                                         |
| gtoccagoco otoctocoto agacocagog gt                                                                                                                                                                                                                                 |                                                          |                                                      |                                                      | 1080                                         |
| cagtgeceee ttgtggeaeg ttgaeceaae et                                                                                                                                                                                                                                 | taccagtt go                                              | gtttttcat                                            | tttttgtccc                                           | 1140                                         |
| tttcccctag atccagaaat aaagtctaag ag aaaaaaaaaa                                                                                                                                                                                                                      | jaagcgcaa aa                                             | aaaaaaaa a                                           |                                                      |                                              |
| <210> 226                                                                                                                                                                                                                                                           |                                                          |                                                      |                                                      | •                                            |
| <211> 119                                                                                                                                                                                                                                                           |                                                          |                                                      |                                                      |                                              |
| <212> DNA                                                                                                                                                                                                                                                           |                                                          |                                                      |                                                      |                                              |
| <213> Homo sapien                                                                                                                                                                                                                                                   |                                                          |                                                      |                                                      |                                              |
| <400> 226                                                                                                                                                                                                                                                           |                                                          |                                                      |                                                      |                                              |
| acccagtatg tgcagggaga cggaacccca tg                                                                                                                                                                                                                                 | tgacagee ea                                              | actccacca d                                          | ggttcccaa                                            | 60                                           |
| agaacctggc ccagtcataa tcattcatcc tg                                                                                                                                                                                                                                 | acagtggc aa                                              | ataatcacg a                                          | ataaccagt                                            | 119                                          |

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<210> 227
      <211> 818
      <212> DNA
      <213> Homo sapien
      <400> 227
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                                                                     60
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                                                                    120
acggacggtt cttagcacaa tttgtgaaat ctgtgtaraa ccgggctttg caggggagat
                                                                    180
aattttcctc ctctggagga aaggtggtga ttgacaggca gggagacagt gacaaggcta
                                                                    240
                                                                    300
gagaaagcca cgctcggcct tctctgaacc aggatggaac ggcagacccc tgaaaacgaa
qcttqtcccc ttccaatcag ccacttctga gaacccccat ctaacttcct actggaaaag
                                                                    360
                                                                    420
agggcctcct caggagcagt ccaagagttt tcaaagataa cgtgacaact accatctaga
qqaaaqqqtq caccctcaqc aqagaaqccg aqagcttaac tctggtcgtt tccagagaca
                                                                    480
                                                                    540
acctgctggc tqtcttggga tqcqcccagc ctttgagagg ccactacccc atgaacttct
qccatccact qqacatqaaq ctqaqqacac tqqqcttcaa cactqaqttq tcatqaqaqq
                                                                    600
gacaggetet geeeteaage eggetgaggg cageaaceae teteeteece ttteteaege
                                                                    660
                                                                    720
aaaqccattc ccacaaatcc agaccatacc atgaagcaac gagacccaaa cagtttggct
caaqaqqata tqaqqactgt ctcagcctgg ctttgggctg acaccatgca cacacacaag
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                                                                    818
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      <211> 744
      <212> DNA
      <213> Homo sapien
      <400> 228
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                                                                    120
                                                                    180
tegtggcega cetggeetet eetggeetgt ttettaagat geggagteae attteaatgg
taggaaaaqt ggcttcqtaa aatagaagag cagtcactgt ggaactacca aatggcgaga
                                                                    240
                                                                    300
tgctcggtgc acattggggt gctttgggat aaaagattta tgagccaact attctctggc
                                                                    360
accagattet aggecagttt gttecaetga agetttteee acageagtee acetetgeag
                                                                    420
qctqqcaqct gaatgqcttq ccgqtqqctc tqtqqcaaga tcacactgag atcgatgqgt
qaqaaqqcta qqatqcttqt ctaqtqttct taqctqtcac gttqqctcct tccaqqttqq
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ccagacggtg ttggccactc ccttctaaaa cacaggcgcc ctcctggtga cagtgacccg
                                                                    540
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ttettttegt taatgtteet etgtgttgte agetgtette attteetggg etaageagea
                                                                    660
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     cttcactctg aagtagctgg tggt
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                                                                     60
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                                                                    120
tgcagggttg ttgtttttta attattattg ttagaaacgt cacccacagt ccctgttaat
                                                                    180
ttgtatgtga cagccaactc tgagaaggtc ctatttttcc acctgcagag gatccagtct
                                                                    240
cactaggete etecttgece teacactgga gteteegeea gtgtgggtge ecactgacat
                                                                    300
      <210> 230
<211> 301
<212> DNA
<213> Homo sapien
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| cagcagaaca aatacaaat                                                                                                                                                            | a tgaagagtgc                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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| gagcgacagt tcaaggagg                                                                                                                                                            | a gaagettgea                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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| caatataaag teetggtte                                                                                                                                                            | a cactcaggaa                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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| cgggaaggga gagatgeet                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      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| gatgaaccgg acaagtccc                                                                                                                                                            | addacadas<br>Google                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  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| g                                                                                                                                                                               | ÷ +                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  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| <210> 231                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      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| <211> 301                                                                                                                                                                       | 20 20 20 20 20                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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| <pre>g</pre>                                                                                                                                                                    | en gctctctaag gtttgatcca tagctggtgc acacagtcac gtagagactt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            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| <pre></pre>                                                                                                                                                                     | en gctctctaag gtttgatcca tagctggtgc acacagtcac gtagagactt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            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| <pre></pre>                                                                                                                                                                     | en gctctctaag gtttgatcca tagctggtgc acacagtcac gtagagactt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            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                                                                                                                                                                                                                                                                                                                                                                              | 301<br>60<br>120<br>180<br>240<br>300<br>301 |
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| <210> 235<br><211> 283<br><212> DNA<br><213> Homo sapien                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <pre>&lt;400&gt; 235 tggggctgtg catcaggcgg gtttgagaaa tattcaattc tcagcagaag ccagaatttg aattccctca tcttttaggg aatcatttac caggtttgga gaggattcag acagctcagg tgctttcact aatgtctctg aacttctgtc cctctttgtt catggatagt ccaataaata atgttatctt tgaactgatg ctcataggag agaatataag aactctgagt gatatcaaca ttagggattc aaagaaatat tagatttaag ctcacactgg tca </pre> <210> 236                                       | 120<br>180                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| <211> 301<br><212> DNA<br><213> Homo sapien                                                                                                                                                                                                                                                                                                                                                         | <b>.</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| <pre>&lt;400&gt; 236 aggtcctcca ccaactgcct gaagcacggt taaaattggg aagaagtata gtgcagcata aatactttta aatcgatcag atttccctaa cccacatgca atcttcttca ccagaagagg tcggagcagc atcattaata ccaagcagaa tgcgtaatag ataaatacaa tggtatatag tgggtagacg gcttcatgag tacagtgtac tgtggtatcg taatctggac ttgggttgta aagcatcgtg taccagtcag aaagcatcaa tactcgacat gaacgaatat aaagaacacc a. </pre> <pre>&lt;210&gt; 237</pre> | 120<br>180<br>240                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| <pre>&lt;213&gt; Homo sapien  &lt;400&gt; 237  cagtggtagt ggtggtggac gtggcgttgg tcgtggtgcc ttttttggtg cccgtcacaa actcaatttt tgttcgctcc tttttggcct tttccaattt gtccatctca atttctggg ccttggctaa tgcctcatag taggagtcct cagaccagcc atggggatca aacatatcct ttgggtagtt ggtgccaagc tcgtcaatgg cacagaatgg atcagcttct cgtaaatcta gggttccgaa attcttctt cctttggata atgtagttca tatccattcc ctcctttatc t</pre>      | 120<br>180<br>240                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| <210> 238<br><211> 301<br><212> DNA<br><213> Homo sapien                                                                                                                                                                                                                                                                                                                                            | ing and the second seco |
| <pre>&lt;400&gt; 238 gggcaggttt ttttttttt ttttttgatg gtgcagaccc ttgctttatt tgtctgactt gttcacagtt cagcccctg ctcagaaaac caacgggcca gctaaggaga ggaggaggca ccttgagact tccggagtcg aggctctcca gggttcccca gcccatcaat cattttctgc acccctgcc tgggaagcag ctccctgggg ggtgggaatg ggtgactaga agggatttca gtgtgggacc cagggtctgt tcttcacagt aggaggtgga agggatgact aatttcttta t</pre>                                 | 120<br>180<br>240                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| <210> 239<br><211> 239<br><212> DNA<br><213> Homo sapien                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |

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| ccgag<br>tgtgg<br>gtctt.<br>cttaa<br>taagt<br>a<br>ggtgg<br>tgacg<br>gctgg                      | <210> 242 <211> 301 <212> DNA <213> Homo sapi <400> 242 gtcct gggatgcaac catt cctcattttc caaga atatatcatt tatca acaaatatat accca aagttttata <210> 243 <211> 301 <212> DNA <213> Homo sapi <400> 243 agtcc cagtttgaag ccaa gctatgaaat tgcag tcggactctg tttgt ccagatggca | en caatcactct tacattgtag cettttcac caagcaaact aatcaaaagc  ctcaaaagat cagagggagg tggcccaagg agacagtaga | gtttcacgtg<br>aatcaagagt<br>tagaaccat<br>ggaaggcaga<br>cctaatgata<br>ctggtatgag<br>cttcatctgg<br>gtatggctct<br>agcagaggct                                                                                                                                                                                                                                                                                                                                                                                                                           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aaggccagga gatattgtca ttaatgtara cttcaggaca ctagagtata gcagccctat
                                                                   180
gttttcaaag agcagagatg caattaaata ttgtttagca tcaaaaaggc cactcaatac
                                                                    240
agctaataaa atgaaagacc taatttctaa agcaattctt tataatttac aaagttttaa
                                                                   300
                                                                    301
      <213> Homo sapien
           ing the first of the second
                                   <400> 246
                                                                    60
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                                                                    120
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                                                                   180
taacaatcat actaaatata ttttgaagta caaagtttga catgctctaa agtgacaacc
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                                                                   120
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                                                                   240
                                                                   300
                                                                   301
а
     <210> 248
<211> 301
<212> DNA
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     <400> 248
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                                                                    120
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| gtacat      | ttcca | gcctgttggc       | aagacagcca<br>aactccataa<br>ttttttatgt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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|             | <210  | > 249            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | and the same of th | Company of the Compan |                   |
|             | <211  | > 301 🔑 📜        | 200 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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|             | <212  | > DNA            | E 1 4 4 7 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 1997 N. 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|             | <213  | > Homo sapi      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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| catco       | Eaato | aattattttg       | aaaattaatt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    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| actga       | atctt | tgactcagaa       | ttgtttgctg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    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| •           | <211  | > 301            | 1 mg 2 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      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| 1.<br>13 *  | <210  | > 252            | and the second s |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            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| ria<br>Gila | <211: | > 301            | 《출고 시민국에 마다워<br>● - 기업 변경 등 기업 등 기업 등                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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|             | <212  | > DNA            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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| : . `       | <213  | > Homo sapi      | ∍n                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            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|             |       | > 252            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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| toatto      | acat  | ttcactacca       | agaguguaaa                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    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                                                                                                                                                                                                                                     | 120               |
| atatat      | Caar  | caaactooss       | acceaticaa                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    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|             |       |                  | atgataacca                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    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| a           |       | <b>-</b>         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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|             |       | e e e            | en e                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | urada en las                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | v.p.n.n. + - 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|             | 221A  | 252              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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      <212> DNA
      <213> Homo sapien
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                                                                    120
tggtctgatt gttttcagac cttaaaatat aaacttgttt cacaagcttt aatccatgtg
                                                                    180
gattttttt cttagagaac cacaaaacat aaaaggagca agtcggactg aatacctgtt
                                                                    240
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                                                                    300
                                                                    301
      <210> 254
      ∠211> 301
      <212> DNA
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      <400> 254
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                                                                    120
ccaaatctct tcatcttacc ctggtggact cctgactgta gaattttttg gttgaaacaa
                                                                    180
gaaaaaaata aagctttgga cttttcaagg ttgcttaaca ggtactgaaa gactggcctc
                                                                    240
acttaaactg agccaggaaa agctgcagat ttattaatgg gtgtgttagt gtgcagtgcc
                                                                    300
                                                                    301
      <210> 255
      <211> 302
      <212> DNA
      <213> Homo sapien
      <400> 255
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attactgaaa tgtttctttt ctgaatataa atataaatat gtgcaaagtt tgacttggat
                                                                    120
tgggattttg ttgagttctt caagcatctc ctaataccct caagggcctg agtaggggg
                                                                    180
aggaaaaagg actggaggtg gaatctttat aaaaaacaag agtgattgag gcagattgta
                                                                    240
aacattatta aaaaacaaga aacaaacaaa aaaatagaga aaaaaaccac cccaacacac
                                                                    300
aa
                                                                    302
      <210> 256
      <211> 301
      <212> DNA
      <213> Homo sapien
                                                1. 2 (1. A.) A. A. A. (1. A.)
                                         1.011 \cdot M_{\odot} \cdot 1.01M_{\odot}
      <220>
      <221> misc feature
      <222> (1)...(301)
      <223> n = A, T, C or G
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                                                                    120
acceccaaaa geetggacae ettgageaea cagttatgae caggacagae teatetetat
                                                                    180
aggcaaatag ctgctggcaa actggcatta cctggtttgt ggggatgggg gggcaagtgt
                                                                    240
gtggcctctc ggcctggtta gcaagaacat tcagggtagg cctaagttan tcgtgttagt
                                                                    300
t.
     <210> 257
                                                                    301
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<211> 301

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<212> DNA
                             <213> Homo sapien
                             <400> 257
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     tocccactta tttttgtott toactatogo aggoottaga agaggtotac otgootocag
                                                                                                                                                                                                                                                                                                    120
     tettacetag tecagtetae eccetggagt tagaatggce atcetgaagt gaaaagtaat
                                                                                                                                                                                                                                                                                                    180
     gtcacattac tcccttcagt gatttcttgt agaagtgcca atccctgaat gccaccaaga
                                                                                                                                                                                                                                                                                                    240
    tettaatett cacatettta atettatete tttgacteet etttacaceg gagaaggete
                                                                                                                                                                                                                                                                                                    300
                               the box of the first the second
                                                                                                                                                                                                                                                                                                   301
                            <210> 258
                            <211> 301
                            <212> DNA
                            <213> Homo sapien
                                                                                                                                                                                                                                                    100
                            <220>
                            <221> misc feature
                            <222> (1) ... (301)
                            <222> (1) • • • (301) \mathbf{r} (223> \mathbf{n} = \mathbf{A}_{\mathbf{r}} \mathbf{T}_{\mathbf{r}} \mathbf{C}_{\mathbf{r}} \mathbf{G}_{\mathbf{r},\mathbf{r}} \mathbf{G}_{\mathbf{r},\mathbf{r}} \mathbf{G}_{\mathbf{r},\mathbf{r},\mathbf{r}} \mathbf{G}_{\mathbf{r},\mathbf{r}} \mathbf{G}_{\mathbf{r},
                                                                  ్ కార్క్ కార్లు కొరియాలు ఉంది.
కార్కు కొరియాలు ఉంది. కార్వార్ కొర్దారు కొరియాలు ప్రామాణ్లు కొరియాలు కొరియాలు
కొరియాలు కొరియాలు కొరియాలు కొరియాలు కొరియాలు కొరియాలు కొరియాలు కొరియాలు కొరియాలు.
                           <400> 258
   cagcagtagt agatgccgta tgccagcacg cccagcactc ccaggatcag caccagcacc 60
   aggggcccag ccaccaggcg cagaagcaag ataaacagta ggctcaagac cagagccacc
   cccagggcaa caagaatcca ataccaggac tgggcaaaat cttcaaagat cttaacactg
   atgtctcggg cattgaggct gtcaataana cgctgatccc ctgctgtatg gtggtgtcat
                                                                                                                                                                                                                                                                                                 240
   tggtgatccc tgggagcgcc ggtggagtaa cgttggtcca tggaaagcag cgcccacaac
                                                                                                                                                                                                                                                                                                 300
                                                                                                                                                                                                                                                                                                 301
                                                                                                                                                                                                                                              Large Corps of Line
                           <210> 259
                          <211> 301
                          <212> DNA
                         <212> DNA
<213> Homo sapien
<220>
<221> misc_feature
<222> (1) ___ (301)
                          <222> (1)...(301)
                          <223> n = A, T, C or G
                          <400> 259
  tcatatatgc aaacaaatgc agactangcc tcaggcagag actaaaggac atctcttggg
                                                                                                                                                                                                                                                                                                     60
  gtgtcctgaa gtgatttgga cccctgaggg cagacaccta agtaggaatc ccagtgggaa
                                                                                                                                                                                                                                                                                                 120
  gcaaagccat aaggaagccc aggattcctt gtgatcagga agtgggccag gaaggtctgt
                                                                                                                                                                                                                                                                                                 180
  tccagctcac atctcatctg catgcagcac ggaccggatg cgcccactgg gtcttggctt
                                                                                                                                                                                                                                                                                                 240
  ccctcccatc ttctcaagca gtgtccttgt tgagccattt gcatccttgg ctccaggtgg
                                                                                                                                                                                                                                                                                                300
                                                                                                                                                                                                                                                                                                 301
                         <210> 260
                         <211> 301
                         <212> DNA ...
                                                                                            Marital and opening the part of the contraction of 
                         <213> Homo sapien
                                                               <400> 260
tttttttttt ccctaaggaa aaagaaggaa caagtctcat aaaaccaaat aagcaatggt
aaggtgtctt aacttgaaaa agattaggag tcactggttt acaagttata attgaatgaa
                                                                                                                                                                                                                                                                                               120.
 agaactgtaa cagccacagt tggccatttc atgccaatgg cagcaaacaa caggattaac
                                                                                                                                                                                                                                                                                               180
tagggcaaaa taaataagtg tgtggaagcc ctgataagtg cttaataaac agactgattc
                                                                                                                                                                                                                                                                                               240
actgagacat cagtacetge eegggeggee getegageeg aattetgeag atatecatea
```

|                                                                |                |             |                                                                                                                                                  | 201        |
|----------------------------------------------------------------|----------------|-------------|--------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| <b>C</b>                                                       | 1              |             |                                                                                                                                                  | 301        |
| <210> 261                                                      |                |             | •                                                                                                                                                |            |
| <211> 301                                                      |                |             |                                                                                                                                                  |            |
| <212> DNA                                                      |                |             |                                                                                                                                                  |            |
| <213> Homo sapien                                              |                |             |                                                                                                                                                  |            |
| <400> 261                                                      | •              |             |                                                                                                                                                  |            |
| aaatattcga gcaaatcctg taactaa                                  | tgt gtctccataa | aaggctttga  | actcagtgaa                                                                                                                                       | 60         |
| tctgcttcca tccacgattc tagcaat                                  | gac ctctcggaca | tcaaagctcc  | tcttaaggtt                                                                                                                                       | 120        |
| agcaccaact attccataca attcatc<br>ggtgacatcc aatttcttct gataatt | agc aggaaataaa | ggctcttcag  | aaggttcaat                                                                                                                                       | 180<br>240 |
| ggcatgatga tcatccaaag cccagtg                                  | otc acttactcca | gactttctgc  | aatgaagatc                                                                                                                                       | 300        |
| a                                                              | <b>J</b>       |             |                                                                                                                                                  | 301        |
|                                                                | •              | •           |                                                                                                                                                  |            |
| <210> 262                                                      | 1              |             |                                                                                                                                                  |            |
| <211> 301<br><212> DNA                                         |                |             |                                                                                                                                                  |            |
| <213> Homo sapien                                              |                |             |                                                                                                                                                  | •          |
| _ '                                                            |                |             | · · ·                                                                                                                                            | 1          |
| <400> 262                                                      |                | 4:<br>      |                                                                                                                                                  |            |
| gaggagagcc tgttacagca tttgtaa<br>tgtgagcttc ttgccgcaag tctctca | gca cagaatactc | caggagtatt  | ctgaattgtc                                                                                                                                       | 60<br>120  |
| cctagacttc ctaaaccaga tectoto                                  | ggg ctggaacctg | gcactctgca  | tttgtaatga                                                                                                                                       | 180        |
| gggctttctg gtgcacacct aattttg                                  | tgc atctttgccc | taaatcctgg  | attagtgccc                                                                                                                                       | 240        |
| catcattacc cccacattat aatggga                                  | tag attcagagca | gatactctcc  | agcaaagaat                                                                                                                                       | 300        |
| C                                                              |                |             |                                                                                                                                                  | 301        |
| <210> 263                                                      |                |             |                                                                                                                                                  |            |
| <211> 301                                                      |                |             | <b>₹</b>                                                                                                                                         |            |
| <212> DNA                                                      |                |             |                                                                                                                                                  | :          |
| <213> Homo sapien                                              |                |             |                                                                                                                                                  |            |
| <220>                                                          |                |             |                                                                                                                                                  | **.        |
| <221> misc_feature                                             |                |             |                                                                                                                                                  | , •        |
| <222> (1) (301) '                                              |                | • • • • • • |                                                                                                                                                  |            |
| <223> n = A, T, C  or  G                                       | :              | 3.          |                                                                                                                                                  |            |
| <400> 263                                                      |                |             |                                                                                                                                                  |            |
| tttagcttgt ggtaaatgac tcacaaa                                  | act gattttaaaa | tcaagttaat  | gtgaattttg                                                                                                                                       | 60         |
| aaaattacta cttaatccta attcaca                                  | ata acaatggcat | taaggtttga  | cttgagttgg .                                                                                                                                     | 120        |
| ttcttagtat tatttatggt aaatagg                                  | ctc ttaccacttg | caaataactg  | gccacatcat                                                                                                                                       | 180<br>240 |
| taatgactga cttcccagta aggctct<br>agatgctaag gccccagaga tcgtttg | cta aggggtaagt | angaggatee  | acaggatte                                                                                                                                        | 300        |
| g                                                              | acc caacccccc  | accccagag   | .gggaaaacggg                                                                                                                                     | 301        |
|                                                                |                |             | ***                                                                                                                                              |            |
| <210> 264                                                      |                |             |                                                                                                                                                  | 1413       |
| <211> 301<br><212> DNA                                         |                |             |                                                                                                                                                  |            |
| <213> Homo sabien                                              |                |             | ego i de tras las productivas.<br>La lata de tras la designa de tras la designa de tras la decimiento de la decimiento de la decimiento de la de | •          |
| <212> DNA<br><213> Homo sapien                                 |                |             | e garagi                                                                                                                                         |            |
| <400> 264                                                      | •              |             |                                                                                                                                                  |            |
| aaagacgtta aaccactcta ctaccac                                  | ttg tggaactctc | aaagggtaaa  | tgacaaascc                                                                                                                                       | 60<br>120  |
| aatgaatgac tetaaaaaca atattta<br>gtggatagat etagaattgt aacattt | taa qaaaaccata | scatttgaca  | gatgagaaag                                                                                                                                       | 180        |
| ctcaattata gatgcaaagt tataact                                  | aaa ctactatagt | agtaaagaaa  | tacatttcac                                                                                                                                       | 240        |
| accettcata taaattcact atcttgg                                  | ctt gaggcactcc | ataaaatgta  | tcacgtgcat                                                                                                                                       | 300        |
| a .                                                            |                |             |                                                                                                                                                  | 301        |

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<210> 265
                 <211> 301
                 <212> DNA
                 <213> Homo sapien
                 <400> 265
  tgcccaagtt atgtgtaagt gtatccgcac ccagaggtaa aactacactg tcatctttgt
                                                                                                                                                                                 60
  cttcttgtga cgcagtattt cttctctggg gagaagccgg gaagtcttct cctggctcta
                                                                                                                                                                               120
  catattettg gaagteteta ateaaetttt gtteeatttg ttteatttet teaggaggga
                                                                                                                                                                               180
  ttttcagttt gtcaacatgt tctctaacaa cacttgccca tttctgtaaa gaatccaaag
                                                                                                                                                                               240
  cagtccaagg ctttgacatg tcaacaacca gcataactag agtatccttc agagatacgg
                                                                                                                                                                               300
                                                                                                                                                                               301
                <210> 266
                 <211> 301
                 <212> DNA
                 <213> Homo sapien
                <400> 266
  taccgtctgc ccttcctccc atccaggcca tctgcgaatc tacatgggtc ctcctaftcg
                                                                                                                                                                                 60
acaccagate actettéet etacecacag gettgetatg ageaagagae acaaceteet
                                                                                                                                                                               120
ctettetgtg ttecagette tittectgtt etteccaece ettaagttet attectgggg
                                                                                                                                                                               180
atagagacae caatacccat aacetetete etaageetee ttataaccca gggtgeacag
                                                                                                                                                                               240
  cacagactee tgacaactgg taaggecaat gaactgggag etcacagetg getgtgeetg
                                                                                                                                                                              300
                  301
                <210> 267
                <211> 301
                <212> DNA
                <213> Homo sapien
                <400> 267
 aaagagcaca ggccagctca gcctgccctg gccatctaga ctcagcctgg ctccatgggg
                                                                                                                                                                                 60
 gttctcagtg ctgagtccat ccaggaaaag ctcacctaga ccttctgagg ctgaatcttc
                                                                                                                                                                               120
 atcotcacag gcagcttotg agagcotgat attoctagco ttgatggtot ggagtaaago
                                                                                                                                                                              180
 ctcattctga ttcctctcct tcttttcttt caagttggct ttcctcacat ccctctqttc
                                                                                                                                                                              240
 aattegette agettgtetg etttageeet cattteeaga agettettet etttggeate
                                                                                                                                                                              300
 t
                                                                                                                                                                              301
                <211> 301 Services of the content of the
                <213> Homo sapien
                <400> 268
 aatgtctcac tcaactactt cccagcctac cgtggcctaa ttctgggagt tttcttctta
                                                                                                                                                                                60
 gatcttggga gagctggttc ttctaaggag aaggaggaag gacagatgta actttggatc
                                                                                                                                                                              120
 tcgaagagga agtctaatgg aagtaattag tcaacggtcc ttgtttagac tcttggaata
                                                                                                                                                                              180
 tgctgggtgg ctcagtgagc ccttttggag aaagcaagta ttattcttaa ggagtaacca
                                                                                                                                                                              240
 cttcccattg ttctactttc taccatcatc aattgtatat tatgtattct ttggagaact
                                                                                                                                                                              300
                                                                                                                                                                              301

    210>. 269
    269
    301
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                <212> DNANTA មាន ពេលមួយ ប៉ុន្តាស់ ១១១៤ មានការ សេសវិទាន់ មន្ត្រាស់សង្គមិន ។
                <213> Homousapien and the secretary services of the contract o
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<400> 269
taacaatata cactagctat ctttttaact gtccatcatt agcaccaatg aagattcaat
                                                                   60
aaaattacct ttattcacac atctcaaaac aattctgcaa attcttagtg aagtttaact
                                                                   120
atagtcacag accttaaata ttcacattgt tttctatgtc tactgaaaat aagttcacta
                                                                  180
cttttctgga tattctttac aaaatcttat taaaattcct ggtattatca cccccaatta
                                                                  240
tacagtagca caaccacctt atgtagtttt tacatgatag ctctgtagaa gtttcacatc
                                                                  300
                                                                   301
      <210> 270
      <211>, 301
      <212> DNA
      <213> Homo sapien
     <400> 270
cattgaagag cttttgcgaa acatcagaac acaagtgctt ataaaattaa ttaagcctta
                                                                   60
cacaagaata catattcctt ttatttctaa ggagttaaac atagatgtag ctgatgtgga
                                                                  120
gagettgetg gtgeagtgea tattggataa cactatteat ggeegaattg atcaagteaa
                                                                  180
ccaactcctt gaactggatc atcagaagaa gggtggtgca cgatatactg cactagataa
                                                                  240
tggaccaacc aactaaattc tctcaccagg ctgtatcagt aaactggctt aacagaaaac
                                                                  300
                                                                   301
      <210> 271
     <211> 301
      <212> DNA
     <213> Homo sapien
     <220>
     <221> misc_feature
     <222> (1)...(301)
     <223> n = A, T, C or G
     <400> 271
aaaaggttct cataagatta acaatttaaa taaatatttg atagaacatt ctttctcatt
                                                                   60
tttatagete atetttaggg ttgatattea gtteatgett ceettgetgt tettgateea
                                                                  120
gaattgcaat cacttcatca gcctgtattc gctccaattc tctataaagt gggtccaagg
                                                                  180
tgaaccacag agccacagca cacctctttc ccttggtgac tgccttcacc ccatganggt
                                                                  240
tototoctoc agatganaac tgatcatgcg cccacatttt gggttttata gaagcagtca
                                                                  300
                                                                  301
     <210> 272
     <211> 301
     <212> DNA
     <213> Homo sapien
                                 <400> 272
taaattgcta agccacagat aacaccaatc aaatggaaca aatcactgtc ttcaaatgtc 60
ttatcagaaa accaaatgag cctggaatct tcataatacc taaacatgcc gtatttagga
tccaataatt ccctcatgat gagcaagaaa aattctttgc gcacccctcc tqcatccaca
gcatcttctc caacaaatat aaccttgagt ggcttcttgt aatctatgtt ctttgttttc
ctaaggactt ccattgcatc tcctacaata ttttctctac gcaccactag aattaagcag
                                                                  301
     <210> 273
     <211> 301
     <212> DNA
     <213> Homo sapien
<220>
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<221> misc feature
               <222> (1) ....(301)
               <222> (1)...(301);
<223> n = A,T,C or G
                                    <400> 273
    acatgtgtgt atgtgtatct ttgggaaaan aanaagacat cttgtttayt atttttttgg 60
    agagangctg ggacatggat aatcacwtaa tttgctayta tyactttaat ctgactygaa
    gaaccgtcta aaaataaaat ttaccatgtc dtatattcct tatagtatgc ttatttcacc
                                                                                                                                        180
   ttytttctgt ccagagagag tatcagtgac ananatttma gggtgaamac atgmattggt
                                                                                                                                        240
   gggacttnty tttacngagm accetgeceg sgegeceteg makengantt ecgesanane
                                                                                                                                        300
                                                                                                                                        301
              <210> 274
             <211> 301
              <222> (1) ... (301)
              <223> n = A, T, C or G
              <400> 274
   cttatatact ctttctcaga ggcaaaagag gagatgggta atgtagacaa ttctttgagg
aacagtaaat gattattaga gagaangaat ggaccaagga gacagaaatt aacttgtaaa
   tgattctctt tggaatctga atgagatcaa gaggccagct ttagcttgtg gaaaagtcca
   totaggtatg gttgcattct cgtcttcttt tctgcagtag ataatgaggt aaccgaaggc
                                                                                                                                       240
   aattgtgctt cttttgataa gaagctttct tggtcatatc aggaaattcc aganaaagtc
                                                                                                   LOWER LABOR SAFRE
                                                                                                                                       301
                                                                                                        1. 1 Sty ...
              <210> 275
              <211> 301
             <212> DNA
<213> Homo sapien
<220>
<221> misc feature
              <212> DNA
             <221> misc_feature
             <222> (1)...(301)
             <223> n = A, T, C or G
             <400> 275
  teggtgteag cagcacgtgg cattgaacat tgcaatgtgg agcccaaacc acagaaaatg
                                                                                                                                         60
  gggtgaaatt ggccaacttt ctattaactt atgttggcaa ttttgccacc aacagtaagc
                                                                                                                                       120
  tggcccttct aataaaagaa aattgaaagg tttctcacta aacggaatta agtagtggag
                                                                                                                                       180
  teaagagact cecaggeete agegtacetg eeegggegge egetegaage egaattetge
                                                                                                                                       240
  agatatecat caeactggeg gnegetegan catgeateta gaaggneeaa ttegeeetat
                                                                                                                                       300
 a
                 ா இது 1778த்து நடித்த இது பெற்றிக்கும் பெற்றிய முற்றிய நடித்து நடித்து
                                                                                                                                       301
  4, 5, 7
             <210> 276 330 7/2/15 this estimate the state of the state
             <211> 301 (1981) (4 1981) (2000) 230 (2000) 250 (2000) (2000)
             <212> DNA
             <213> Homo sapien
             <400> 276
 tgtacacata ctcaataaat aaatgactgc attgtggtat tattactata ctgattatat
                                                                                                                                        60
  ttatcatgtg acttctaatt agaaaatgta tccaaaagca aaacagcaga tatacaaaat
                                                                                                                                      120
  taaagagaca gaagatagac attaacagat aaggcaactt atacattgag aatccaaatc
                                                                                                                                      180
  caatacattt aaacatttgg gaaatgaggg ggacaaatgg aagccagatc aaatttgtgt
                                                                                                                                      240
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aaaactattc agtatgtttc ccttgcttca tgtctgagaa ggctctcctt caatggggat
                                                                                                                                                                    300
                                                                                                                                                                    301
           <210> 277
              <211> 301
              <212> DNA
              <213> Homo sapien
              <220>
              <221> misc feature
              <222> (1) ... (301)
              <223> n = A, T, C or G
            <400> 277
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atacagagga cttggaggaa gcagagcaac tgaatttaat ttaaaagaag gaaaacattg
                                                                                                                                                                    120
gaatcatggc actoctgata ctttcccaaa tcaacactct caatgcccca ccctcgtcct
                                                                                                                                                                    180
caccatagtg gggagactaa agtggccacg gatttgcctt angtgtgcag tgcgttctga
                                                                                                                                                                    240
gttenetgte gattacatet gaccagtete ettttteega agteenteeg tteaatettg
                                                                                                                                                                    300
                                                                                                                                                                    301
              <210> 278
              <211> 301
              <212> DNA
             <213> Homo sapien
              <220>
              <221> misc_feature
              <222> (1)...(301)
              <223> n = A, T, C \text{ or } G
taccactaca ctccagcctg ggcaacagag caagacctgt ctcaaagcat aaaatggaat
aacatatcaa atgaaacagg gaaaatgaag ctgacaattt atggaagcca gggcttgtca
                                                                                                                                                                    120
cagtetetac tgttattatg cattacetgg gaatttatat aageeettaa taataatgee
                                                                                                                                                                    180
aatgaacatc tcatgtgtgc tcacaatgtt ctggcactat tataagtgct tcacaggttt
                                                                                                                                                                    240
tatgtqttct tcqtaacttt atggantagg tactcggccg cgaacacgct aagccgaatt
                                                                                                                                                                    300
                                                                                                                                                                    301
              <210> 279
              <211> 301
              <212> DNA
              <213> Homo sapien
              <220>
                                                                                                                             The state of the s
              <221> misc feature
              <222> (1)...(301)
                                                                                                                            military from the second
              <223> n = A, T, C or G
              <400> 279
aaagcaggaa tgacaaagct tgcttttctg gtatgttcta ggtgtattgt gacttttact
                                                                                                                                                                     60
qttatattaa ttgccaatat aagtaaatat agattatata tgtatagtgt ttcacaaagc
                                                                                                                                                                    120
ttagaccttt accttccagc caccccacag tgcttgatat ttcagagtca gtcattggtt
                                                                                                                                                                    180
atacatqtqt aqttccaaag cacataagct agaanaanaa atatttctag ggagcactac
                                                                                                                                                                    240
catctqtttt cacatqaaat qccacacaca tagaactcca acatcaattt cattqcacag
                                                                                                                                                                    300
                                                                                                                                                                    301
а
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<211> 301
                 <212> DNA
                 <213> Homo sapien
                 <400> 280
    ggtactggag ttttcctccc ctgtgaaaac gtaactactg ttgggagtga attgaggatg
                                                                                                                                                        60
    tagaaaggtg gtggaaccaa attgtggtca atggaaatag gagaatatgg ttctcactct
                                                                                                                                                      120
    tgagaaaaaa acctaagatt agcccaggta gttgcctgta acttcagttt ttctgcctgg
   gtttgatata gtttagggtt ggggttagat taagatctaa attacatcag gacaaagaga
                                                                                                                                                      240
    cagactatta actocacagt taattaagga ggtatgttcc atgtttattt gttaaagcag
                                                                                                                                                      300
                                                                                                             100
                                                                                                                                                      301
                                                                                                      to the form of the state of
                 <210> 281
                 <211> 301
                <213> Homo sapien
<400> 281
               ►<212> DNA
    <400> 281
aggtacaaga aggggaatgg gaaagagetg ctgctgtggc attgttcaac ttggatattc 60
    geogageaat ceaaateetg aatgaagggg catettetga aaaaggagat etgaatetea
   atgtggtagc aatggcttta tcgggttata cggatgagaa gaactccctt tggagagaaa
                                                                                                                                                     180
    tgtgtagcac actgcgatta cagctaaata acccgtattt gtgtgtcatg tttgcatttc
                                                                                                                                                      240
    tgacaagtga aacaggatct tacgatggag ttttgtatga aaacaaagtt gcagtacctc
                                                                                                                                                      300
    g :
                                                                                                                                                      301
                <210> 282
                <211> 301
                                                                                                                                       \mathcal{A}_{\mathcal{A}}(\mathcal{A}, \mathcal{R}, \mathcal{P}_{\mathcal{A}})
                <212> DNA
                                                                                                            State of the State
                <213> Homo sapien
                                                                                                             JAN 1.1 (11 HAS)
                                                                                                            <400> 282
    caggtactac agaattaaaa tactgacaag caagtagttt cttggcgtgc acgaattgca
                                                                                                                                                        60
    tccagaaccc aaaaattaag aaattcaaaa agacattttg tgggcacctg ctagcacaga
                                                                                                                                                      120
    agogoagaag caaagoocag goagaaccat gotaacctta cagotoagoo tgcacagaag
                                                                                                                                                      180
    cgcagaagca aagcccaggc agaaccatgc taaccttaca gctcagcctg cacagaagcg
                                                                                                                                                     240
    cagaagcaaa gcccaggcag aacatgctaa ccttacagct cagcctgcac agaagcacag
                                                                                                                                                     300
                                                                                                                                                     301
......a. .∵
                <210> 283
                <211> 301
                <212> DNA
                <213> Homo sapien
                <400> 283
    atctgtatac ggcagacaaa ctttatarag tgtagagagg tgagcgaaag gatgcaaaag
                                                                                                                                                        60
    cactttgagg gctttataat aatatgctgc ttgaaaaaaa aaatgtgtag ttgatactca
                                                                                                                                                     120
   gtgcatetce agacatagta aggggttgct etgaceaate aggtgateat tttttetate
                                                                                                                                                     180
   acttcccagg ttttatgcaa aaattttgtt aaattctata atggtgatat gcatctttta
                                                                                                                                                     240
   ggaaacatat acatttttaa aaatctattt tatgtaagaa ctgacagacg aatttgcttt
                                                                                                                                                     300
   g
                                                                                                                                                     301
                                       ្នាក់ ស្ថិត្ត ទៅពី សក្សា ក្រុម សក្សាទីក្រុម ប្រុស្ធាន ស្ថិត្តិសុខ សក្សាទីក្រុម ស្ថិត្តិសុខ សិក្សាទីកុំពីសភាពល
ការស្វេស ស្ថិត សុខ ទីកិន្តិសុខសុខិស្សិក សក្សាទីកុំពីសភាពសុខសុខិស្សិក សក្សាទីកុំពី ឯងសារីសុខិស្សិក សុ
                <210> 284
               <211> 301
               caggiacaaa acgciattaa giggciiaga attigaacai tigiggicti tattiactii,
                                                                                                                                                       60
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gcttcgtgtg tgggcaaagc aacatcttcc ctaaatatat attaccaaga aaagcaagaa
                                                                      120
gcagattagg tttttgacaa aacaaacagg ccaaaagggg gctgacctgg agcagagcat
                                                                      180
ggtgagaggc aaggcatgag agggcaagtt tgttgtggac agatctgtgc ctactttatt
                                                                      240
actggagtaa aagaaaacaa agttcattga tgtcgaagga tatatacagt gttagaaatt
                                                                      300
                                                                      301
      <210> 285
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220> '
      <221> misc_feature
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      <223> n = A,T,C or G
      <400> 285
acatcaccat gatcggatcc cccacccatt atacgttgta tgtttacata aatactcttc
                                                                       60
aatgatcatt agtgttttaa aaaaaatact gaaaactcct tctgcatccc aatctctaac
                                                                      120
caggaaagca aatgctattt acagacctgc aagccctccc tcaaacnaaa ctatttctgg
                                                                      180
attaaatatg tetgaettet tittgaggtea caegaetagg caaatgetat titaegatetg
                                                                      240
caaaagctgt ttgaagagtc aaagccccca tgtgaacacg atttctggac cctgtaacag
                                                                      300
                                                                      301
      <210> 286
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 286
taccactgca ttccagcctg ggtgacagag tgagactccg tctccaaaaa aaactttgct
tgtatattat ttttgcctta cagtggatca ttctagtagg aaaggacagt aagatttttt
                                                                      120
atcaaaatgt gtcatgccag taagagatgt tatattcttt tctcatttct tccccaccca
                                                                      180
aaaataagct accatatagc ttataagtct caaatttttg ccttttacta aaatgtgatt
                                                                      240
gtttetgtte attgtgtatg ctteateace tatattagge aaatteeatt tttteeettg
                                                                      300
      <210> 287
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 287
tacagatotg ggaactaaat attaaaaatg agtgtggctg gatatatgga gaatgttggg
                                                                       60
cccagaagga acgtagagat cagatattac aacagctttg ttttgagggt tagaaatatg
                                                                      120
aaatgatttg gttatgaacg cacagtttag gcagcagggc cagaatcctg accetetgce
                                                                      180
ccgtggttat ctcctccca gcttggctgc ctcatgttat cacagtattc cattitgttt
                                                                      240
gttgcatgtc ttgtgaagcc atcaagattt tctcgtctgt tttcctctca ttggtaatgc
                                                                      300
                                                                      301
      <210> 288
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 288
gtacacctaa ctgcaaqqac agctgaggaa tgtaatgggc agccgctttt aaaqaaqtaq
                                                                       60
agtcaatagg aagacaaatt ccagttccag ctcagtctgg gtatctgcaa agctgcaaaa
                                                                      120
```

```
qatctttaaa gacaatttca agagaatatt toottaaagt tggcaatttg gagatcatac
aaaagcatct gcttttgtga tttaatttag ctcatctggc cactggaaga atccaaacag
                                                                 300
tctgccttaa ttttggatga atgcatgatg gaaattcaat aatttagaaa gttaaaaaaa
                                                                 301
     <210> 289
     <211> 301
     <212> DNA
     <213> Homo sapien
     <220> ,
     <221> misc_feature
     <222> (1) ... (301)
     <223> n = A,T,C or G
     <400> 289
qqtacactqt ttccatqtta tqtttctaca cattqctacc tcagtqctcc tggaaactta
gettttgatg tetecaagta gtecacette atttaactet ttgaaactgt atcatetttg 120
ccaagtaaga gtggtggcct atttcagctg ctttgacaaa atgactggct cctgacttaa
cgttctataa atgaatgtgc tgaagcaaag tgcccatggt ggcggcgaan aagagaaaga
                                                                 300
tgtgttttgt tttggactet etgtggteec tteeaatget gtgggtttee aaccagngga
                                                                 301
                        ş 2.
                            10.00
                                 7.7
     <210> 290
     <211> 301
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc_feature
     <222> (1)...(301)
     <223> n = A, T, C or G
     <400> 290
acactgaget cttetigata aatatacaga atgettggea tatacaagat tetatactac
                                                                  60
tgactgatet gttcatttct ctcacagete ttacceccaa aagettttee accetaagtg
                                                                 120
                                                                 180
ttctgacctc cttttctaat cacagtaggg atagaggcag anccacctac aatgaacatg
gagttctatc aagaggcaga aacagcacag aatcccagtt ttaccattcg ctagcagtgc
                                                                 240
                                                                 300
tgccttgaac aaaaacattt ctccatgtct cattttcttc atgcctcaag taacagtgag
                                                                 301
     <210> 291
     <211> 301
     <212> DNA
                      COUNTRY 1920 COMPLETED AND AND A
     <213> Homo sapien
              THE PHOUSE PARTY OF THE EAST
     <400> 291
caggtaccaa tttcttctat cctagaaaca tttcatttta tgttgttgaa acataacaac
                                                                  60
tatatcagct agatttttt tctatgcttt acctgctatg gaaaatttga cacattctgc
                                                                 120
tttactcttt tgtttatagg tgaatcacaa aatgtatttt tatgtattct gtagttcaat
                                                                 180
agccatggct gtttacttca tttaatttat ttagcataaa gacattatga aaaggcctaa
                                                                 240
                                                                 300
acatgagett cactteecca etaactaatt ageatetgtt atttettaac egtaatgeet.
                                                       The second second
                                                公告 医二乙酰因 不经产品
     <210> 292
     <211> 301
```

```
<220>
      <221> misc feature
      <222> (1) ... (301)
      <223> n = A, T, C or G
      <400> 292
accttttagt agtaatgtct aataataaat aagaaatcaa ttttataagg tccatatagc
                                                                 60
tgtattaaat aatttttaag tttaaaagat aaaataccat cattttaaat gttggtattc
                                                                120
, aaaaccaaag natataaccg aaaggaaaaa cagatgagac ataaaatgat ttgcnagatg
                                                                180
ggaaatatag tasttyatga atgttnatta aattccagtt ataatagtgg ctacacactc
                                                                240
tcactacaca cacagacccc acagtectat atgecacaaa cacattteca taacttgaaa
                                                                300
                                                                301
     <210> 293
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 293
ggtaccaagt gctggtgcca gcctgttacc tgttctcact gaaaagtctg gctaatgctc
                                                                 60
ttqtqtaqtc acttctgatt ctgacaatca atcaatcaat ggcctagagc actgactgtt
                                                                120
aacacaaacg tcactagcaa agtagcaaca gctttaagtc taaatacaaa gctgttctgt
                                                                180
gtgagaattt tttaaaaggc tacttgtata ataacccttg tcatttttaa tgtacctcgg
                                                                240
cegegaceae getaageega attetgeaga tatecateae aetggeggee getegageat
                                                                300
      <210> 294
<211> 301
                                                                301
g
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(301)
      <223> n = A, T, C or G
      <400> 294
                                                                 60
tgacccataa caatatacac tagctatctt tttaactgtc catcattagc accaatgaag
attcaataaa attaccttta ttcacacatc tcaaaacaat tctgcaaatt cttagtgaag
                                                                120
tttaactata gtcacaganc ttaaatattc acattgtttt ctatgtctac tgaaaataag
                                                                180
ttcactactt ttctgggata ttctttacaa aatcttatta aaattcctgg tattatcacc
                                                                240
cccaattata cagtagcaca accaccttat gtagttttta catgatagct ctgtagaggt
                                                                300
                        ے عمل
                                                                301
                      <210> 295
      <211> 305
      <212> DNA
      <213> Homo sapien
      <400> 295
gtactettte teteceetee tetgaattta attettteaa ettgeaattt geaaggatta
                                                                 60
 120
ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga
                                                                180
 actggtagaa aaacrtctga agagctagtc tatcagcatc tgacaggtga attggatggt
                                                                240
tctcagaacc atttcaccca gacagcctgt ttctatcctg tttaataaat tagtttgggt
                                                                300
                                                                305
 tctct
```

and the state of t

```
<210> 296
               <211> 301
                <212> DNA
                <213> Homo sapien
               <400> 296
   aggtactatg ggaagctgct aaaataatat ttgatagtaa aagtatgtaa tgtgctatct
                                                                                                                                                     60
cacctagtag taaactaaaa ataaactgaa actttatgga atctgaagtt attttccttg
 attaaataga attaataaac caatatgagg aaacatgaaa ccatgcaatc tactatcaac
   tttgaaaaag tgattgaacg aaccacttag ctttcagatg atgaacactg ataaqtcatt
   tgtcattact ataaatttta aaatctgtta ataagatggc ctatagggag gaaaaagggg
   C
               <210> 297
              <211> 300
                                                                                                                          A. 4.1553
               <212> DNA
                                                                                                                        (X_{2}^{-1})_{1} = (S_{2})_{A_{1} = A_{2}}
               <213> Homo sapien
               <220>
              <221> misc_feature <222> (1)...(300)
                                                            the same of the
               \langle 223 \rangle n = A, T, C or G
                                  the first of the second of the constraint which is a second of the constraint.
              <400> 297..., ...,
                                                      actgagtttt aactggacgc caagcaggca aggctggaag gttttgctct ctttgtgcta
   aaggttttga aaaccttgaa ggagaatcat tttgacaaga agtacttaag agtctagaga
                                                                                                                                                  120
   acaaagangt gaaccagctg aaagctctcg ggggaanctt acatgtgttg ttaggcctgt
                                                                                                                                                  180
   tocatcattg ggagtgcact ggccatccct caaaatttgt ctgggctggc ctgagtggtc
                                                                                                                                                  240
   accgcacctc ggccgcgacc acgctaagcc gaattctgca gatatccatc acactggcgg
                                                                                                                                                  300
               <210> 298
               <211> 301
               <212> DNA
               <213> Homo sapien
              <220>
              <221> misc feature
              <222> (1)...(301)
              \langle 223 \rangle n = A,T,C or G
              <400> 298
  tatggggttt gtcacccaaa agctgatgct gagaaaggcc tccctggggc ccctcccgcg
  ggcatctgag agacctggtg ttccagtgtt tctggaaatg ggtcccagtg ccgccggctg
                                                                                                                                                  120
  tgaagctctc agatcaatca cgggaagggc ctggcggtgg tggccacctg gaaccaccct
                                                                                                                                                 180
  gtcctgtctg tttacatttc actaycaggt tttctctggg cattacnatt tgttcccta
                                                                                                                                                 240
  caacagtgac ctgtgcattc tgctgtggcc tgctgtgtct gcaggtggct ctcaqcqaqq
                                                                                                                                                 300
                                                                                                                                                 301
              <210> 299
              <211> 301
              <212> DNA
              un distriction in a my factor of the Adult to the Cities of Giller
Charles and the Company of the State of the Company of the 
              <400> 299
  gttttgagac ggagtttcac tcttgttgcc cagactggac tgcaatggca gggtctctgc
  teactgeace etetgeetee caggitegag caatteteet geeteageet eccaggtage
                                                                                                                                            120
  tgggattgca ggctcacgcc accataccca gctaattttt ttgtattttt agtagagacg
                                                                                                                                                 180
  gagtttcgcc atgttggcca gctggtctca aactcctgac ctcaagcgac ctgcctgcct
```

| cggcctccca aagtgctgga at | tataggca    | tgagtcaaca                            | cgcccagcct                       | aaagatattt | 300                                      |
|--------------------------|-------------|---------------------------------------|----------------------------------|------------|------------------------------------------|
| t                        |             |                                       |                                  |            | 301                                      |
| 4,                       |             |                                       |                                  | •          |                                          |
| <210> 300                |             | •                                     | . •                              | •          |                                          |
| <211> 301                | 1           |                                       |                                  | •          |                                          |
| <212> DNA                | . 9         | 2                                     | • •                              |            |                                          |
| <213> Homo sapien        | *           |                                       |                                  |            | •                                        |
|                          |             | `:                                    | •                                |            | *                                        |
| <400> 300                |             |                                       |                                  |            | •                                        |
| attcagtttt atttgctgcc cc |             |                                       |                                  |            | 60                                       |
| tatgtcccac acccactggg aa |             |                                       |                                  |            | 120                                      |
| gctgcattcc acaaggttct ca |             |                                       |                                  |            | 180                                      |
| gtaaagcaag accatgacat to | ccccacgg    | aaatcagagt                            | ttgccccacc                       | gtcttgttac | 240                                      |
| tataaagcet geetetaaca gt | ccttgctt    | cttcacacca                            | atcccgagcg                       | catcccccat | 300                                      |
| g                        | •           |                                       |                                  |            | 301                                      |
| 1                        |             |                                       |                                  | * :        |                                          |
| <210> 301                | ,           |                                       | ;                                |            |                                          |
| <211> 301                |             |                                       |                                  |            |                                          |
| <212> DNA                |             |                                       | A                                | • •        |                                          |
| <213> Homo sapien        |             |                                       |                                  |            |                                          |
| r                        |             |                                       | 1                                |            | 1                                        |
| <400> 301                |             |                                       | r e e                            |            |                                          |
| ttaaattttt gagaggataa aa | aggacaaa    | taatctagaa                            | atotototto                       | ttcagtctgc | 60                                       |
| agaggacccc aggtctccaa gc |             |                                       |                                  |            | 120                                      |
| gggaactcac aaagaccctc ag |             |                                       |                                  |            |                                          |
| ctcagagctg agacacccac aa |             |                                       |                                  |            | 240                                      |
| cacaacagca cetegtteag et |             |                                       |                                  |            | 300                                      |
| t                        | .,          | -,-,                                  | 3009000090                       | ocaguagugo | 301                                      |
| _                        |             |                                       |                                  |            | 552                                      |
| <210> 302                |             |                                       |                                  |            |                                          |
| <211> 301                |             |                                       |                                  |            | i                                        |
| <212> DNA                |             |                                       | £                                |            |                                          |
| <213> Homo sapien        |             |                                       |                                  |            |                                          |
| 12132 Nomo Sapien        |             |                                       |                                  |            |                                          |
| <400> 302                |             |                                       |                                  |            | 28-4                                     |
| aggtacacat ttagcttgtg gt | aaataact    | cacaaaacto                            | attttaaaat                       | caacttaato | 60                                       |
| tgaattttga aaattactac tt |             |                                       |                                  |            | 120                                      |
| ttgagttggt tcttagtatt at |             |                                       |                                  |            | 180                                      |
| ccacatcatt aatgactgac tt |             |                                       |                                  |            |                                          |
| caggatttga gatgctaagg co |             |                                       |                                  |            | 240                                      |
|                          | ccayagat    | cgtttgatee                            | aaccetetta                       | ttttcagagg | 300                                      |
| g .                      |             |                                       |                                  | •          | 301                                      |
| ∠210 <u>&gt;</u> 202     |             |                                       |                                  |            | •.                                       |
| <210> 303<br><211> 301   |             |                                       |                                  |            |                                          |
|                          | •           |                                       | •                                |            |                                          |
| <212> DNA                | •           |                                       | Participation of the Western Co. |            | en e |
| <213> Homo sapien        |             | · · · · · · · · · · · · · · · · · · · |                                  | •          |                                          |
| 4400 000                 | • • • • • • |                                       |                                  |            |                                          |
| <400> 303                |             |                                       |                                  |            |                                          |
| aggtaccaac tgtggaaata gg |             |                                       |                                  |            |                                          |
| atattgtttt ttgacagttt aa | cacatett    | cttctgtcag                            | agattette                        | acaatagcac | 120                                      |
| tggctaatgg aactaccgct tg |             |                                       |                                  |            | 180                                      |
| agtaacgggt atgttttct aa  |             |                                       |                                  |            | 240                                      |
| catcgatttt atatctgggg to | tagaaaag    |                                       |                                  | ataaattcac | 300                                      |
| C                        |             |                                       |                                  |            | 301                                      |
|                          | -           |                                       |                                  |            |                                          |
| <210> 304                |             | •                                     |                                  |            |                                          |
| <211> 301                |             |                                       |                                  |            | ,                                        |
| <212> DNA                |             |                                       |                                  |            | •                                        |
|                          | •           |                                       |                                  |            |                                          |

```
<213> Homo sapien
                             <400> 304
      acatogatot tattitiqua actoticaace togattiqua titiquitique attocctaat
                                                                                                                                                                                                                                                                                        60
      tattagtttc agtttcagct tacccacttt ttgtctgcaa catgcaraas agacagtgcc
                                                                                                                                                                                                                                                                                    120
      ctttttagtg tatcatatca ggaatcatct cacattggtt tgtgccatta ctggtgcagt
                                                                                                                                                                                                                                                                                    180
      gactttcagc cacttgggta aggtggagtt ggccatatgt ctccactgca aaattactga
                                                                                                                                                                                                                                                                                    240
      ttttcctttt gtaattaata agtgtgtgtg tgaagattct ttgagatgag gtatatatct
                                                                                                                                                                                                                                                                                    300
                                                                                                                                                                                                                                                                                    301
   ·C
                             <210> 305
                             <210> 305 cm to a roll and to the roll of the control of the contr
                             <212> DNA de montre repris de la della del
                             <220>
                             <221> misc feature
                             <222> (1)...(301)
                             <223> n = A, T, C \text{ or } G
                             <400> 305
      gangtacago gtggtcaagg taacaagaag aaaaaaatgt gagtggcatc ctgggatgag
      cagggggaca gacctggaca gacacgttgt catttgctgc tgtgggtagg aaaatgggcg . 120
      taaaggagga gaaacagata caaaatctcc aactcagtat taaggtattc tcatgcctag
                                                                                                                                                                                                                                                                                   180
                                                                                                                                                                                                                                                                                   240
      aatattggta gaaacaagaa tacattcata tggcaaataa ctaaccatgg tggaacaaaa
      ttctgggatt taagttggat accaangaaa ttgtattaaa agagctgttc atggaataag
                                                                                                                                                                                                                                                                                   300
                                          in the company of the control of the
                                                                                                                                                                                                                                                                                   301
                             <210> 306
                             <211> 8
                                                                                                                                                                                                                                        <212> PRT
                             <213> Homo sapien
                             <400> 306
      Val Leu Gly Trp Val Ala Glu Leu
                           1
                     4,22
٠, ١,
                            <213> Homo sapien
                             <400> 307
     acagggratg aagggaaagg gagaggatga ggaagccccc ctggggattt ggtttggtcc
                                                                                                                                                                                                                                                                                     60
     ttgtgatcag gtggtctatg gggcttatcc ctacaaagaa gaatccagaa ataggggcac
                                                                                                                                                                                                                                                                                   120
     attgaggaat gatacttgag cccaaagagc attcaatcat tgttttattt gccttmtttt
                                                                                                                                                                                                                                                                                   180
     cacaccattg gtgagggagg gattaccacc ctggggttat gaagatggtt gaacacccca
                                                                                                                                                                                                                                                                                   240
     cacatagcac cggagatatg agatcaacag tttcttagcc atagagattc acagcccaga
                                                                                                                                                                                                                                                                                   300
    gcaggaggac gcttgcacac catgcaggat gacatggggg atgcgctcgg gattggtgtg
                                                                                                                                                                                                                                                                                   360
     aagaagcaag gactgttaga ggcaggcttt atagtaacaa gacggtgggg caaactctga 420
     tttccqtqqq qqaatqtcat; qqtcttqctt tactaaqttt tqaqactqqc aggtaqtqaa
                                                                                                                                                                                                                                                                                   480
     actcattagg ctgagaacct tgtggaatgc acttgaccca sctgatagag gaagtagcca
                                                                                                                                                                                                                                                                         540
     ggtgggagcc tttcccagtg ggtgtgggac atatctggca agattttgtg gcactcctgg
                                                                                                                                                                                                                                                                               600
     ttacagatac tggggcagca aataaaactg aatcttg
                                                                                                                                                                                                                                                                                   637
                            <210> 308
                                                                                                                                                                                                                                         8 18 July 19
                            <211> 647
```

<212> DNA

```
<213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(647)
      <223> n = A, T, C or G
      <400> 308
acgattttca ttatcatgta aatcgggtca ctcaaggggc caaccacagc tgggagccac
                                                                        60
tgctcagggg aaggttcata tgggactttc tactgcccaa ggttctatac aggatataaa
                                                                       120
ggngcctcac agtatagatc tggtagcaaa gaagaagaaa caaacactga tctctttctg
                                                                      180
                                                                       240
ccacccctct gaccctttgg aactcctctg accetttaga acaagcctac ctaatatctg
                                                                       300
ctagagaaaa gaccaacaac ggcctcaaag gatctcttac catgaaggtc tcagctaatt
                                                                       360
cttggctaag atgtgggttc cacattaggt tctgaatatg gggggaaggg tcaatttgct
cattttgtgt gtggataaag tcaggatgcc caggggccag agcagggggc tgcttgcttt
                                                                       420
gggaacaatg gctgagcata taaccatagg ttatggggaa caaaacaaca tcaaagtcac
                                                                       480
tgtatcaatt gccatgaaga cttgagggac ctgaatctac cgattcatct taaggcagca
                                                                       540
ggaccagttt gagtggcaac aatgcagcag cagaatcaat ggaaacaaca gaatgattgc
                                                                       600
                                                                       647
aatgtccttt tttttctcct gcttctgact tgataaaagg ggaccgt
      <210> 309
      <211> 460
      <212> DNA
      <213> Homo sapien
                   <400> 309
actttatagt ttaggctgga cattggaaaa aaaaaaaagc cagaacaaca tgtgatagat
                                                                        60
aatatgattg gctgcacact tccagactga tgaatgatga acgtgatgga ctattgtatg
                                                                       120
gagcacatct tcagcaagag ggggaaatac tcatcatttt tggccagcag ttgtttgatc
                                                                       180
accaaacatc atgccagaat actcagcaaa ccttcttagc tcttgagaag tcaaagtccg
                                                                       240
ggggaattta ttcctggcaa ttttaattgg actccttatg tgagagcagc ggctacccag
                                                                       300
ctggggtggt ggagcgaacc cgtcactagt ggacatgcag tggcagagct cctggtaacc
                                                                       360
                                                                       420
acctagagga atacacaggc acatgtgtga tgccaagcgt gacacctgta gcactcaaat
ttgtcttgtt tttgtctttc ggtgtgtaag attcttaagt
                                                                       460
      <210> 310
      <211> 539
      <212> DNA
      <213> Homo sapien
      <400> 310
                                                                        60
acgggactta tcaaataaag ataggaaaag aagaaaactc aaatattata ggcagaaatg
ctaaaggttt taaaatatgt caggattgga agaaggcatg gataaagaac aaagttcagt
                                                                       120
                                                                       180
taggaaagag aaacacagaa ggaagagaca caataaaagt cattatgtat tctgtgagaa
gtcagacagt aagatttgtg ggaaatgggt tggtttgttg tatggtatgt attttagcaa
                                                                       240
taatctttat ggcagagaaa gctaaaatcc tttagcttgc gtgaatgatc acttgctgaa
                                                                       300
ttcctcaagg taggcatgat gaaggaggt ttagaggaga cacagacaca atgaactgac
                                                                       360
                                                                       420
ctagatagaa agccttagta tactcagcta ggaatagtga ttctgagggc acactgtgac.
atgattatgt cattacatgt atggtagtga tggggatgat aggaaggaag aacttatggc
                                                                       480
atattttcac ccccacaaaa gtcagttaaa tattgggaca ctaaccatcc aggtcaaga
                                                                       539
      <210> 311
      <211> 526
      <212> DNA
      <213> Homo sapien
11
      <220>
      <221> misc feature
```

<222> (1) ... (526)

```
<223> n = A,T,C or G
        <400> 311
  caaatttgag ccaatgacat agaattttac aaatcaagaa gcttattctg gggccatttc
                                                                         60
  ttttgacgtt ttctctaaac tactaaagag gcattaatga tccataaatt atattatcta
                                                                        120
  catttacagc atttaaaatg tgttcagcat gaaatattag ctacagggga agctaaataa
                                                                        180
  attaaacatg gaataaagat tigtccitaa atataatcta caagaagact tigatattig
                                                                        240
  tttttcacaa gtgaagcatt cttataaagt gtcataacct ttttggggaa actatgggaa
                                                                        300
  aaaatgggga aactctgaag ggttttaagt atcttacctg aagctacaga ctccataacc
                                                                        360
  tetetttaca gggageteet geageeeta cagaaatgag tggetgagat tettgattge
                                                                        420
  acagcaagag cttctcatct aaaccctttc cctttttagt atctgtgtat caagtataaa
                                                                        480
  agttctataa actgtagtnt acttatttta atccccaaag cacagt
                                                                        526
       *<210> 312
        <211> 500
<212> DNA
        <213> Homo sapien
       <220>
        <221> misc feature
        <222> (1)...(500)
        <223> n = A, T, C or G
        <400> 312
  cetetetete eccaecect gaetetagag aactgggttt teteceagta etccagcaat
                                                                         60
  teatttetga aageagttga gecaetttat tecaaagtae aetgeagatg tteaaactet
                                                                        120
  ccatttctct ttcccttcca cctgccagtt ttgctgactc tcaacttgtc atgagtgtaa
                                                                        180
  gcattaagga cattatgctt cttcgattct gaagacaggc cctgctcatg gatgactctg
                                                                        240
  gcttcttagg aaaatatttt tcttccaaaa tcagtaggaa atctaaactt atccctctt
                                                                        300
  tgcagatgtc tagcagcttc agacatttgg ttaagaaccc atgggaaaaa aaaaaatcct
                                                                        3.60
  tgctaatgtg gtttcctttg taaaccanga ttcttatttg nctggtatag aatatcagct
                                                                        420
 ctgaacgtgt ggtaaagatt tttgtgtttg aatataggag aaatcagttt gctgaaaagt
                                                                        480
  tagtcttaat tatctattgg
                                                                        500
       <210> 313
       <211> 718
       <212> DNA
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       <220>
       <221> misc_feature
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       <223> n = A, T, C \text{ or } G
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 ggagatttgt gtggtttgca gccgagggag accaggaaga tctgcatggt gggaaggacc
                                                                         60
tgatgataca gaggtgagaa ataagaaagg ctgctgactt taccatctga ggccacacat
                                                                        120
ctgctgaaat ggagataatt aacatcacta gaaacagcaa gatgacaata taatgtctaa
                                                                        180
 gtagtgacat gtttttgcac atttccagcc cttttaaata tccacacaca caggaagcac
                                                                        240
 aaaaggaagc acagagatcc ctgggagaaa tgcccggccg ccatcttggg tcatcgatga
                                                                        300
 geotegeect gtgeetgnte eegettgtga gggaaggaca ttagaaaatg aattgatgtg
                                                                        360
 ttccttaaag gatggcagga aaacagatcc tgttgtggat atttatttga acgggattac
                                                                        420
 agatttgaaa tgaagtcaca aagtgagcat taccaatgag aggaaaacag acgagaaaat
                                                                        480
 cttgatggtt cacaagacat gcaacaaaca aaatggaata ctgtgatgac acgagcagcc
                                                                        540
 aactggggag gagataccac ggggcagagg tcaggattct ggccctgctg cctaactgtg
                                                                        600
 cgttatacca atcattcta tttctaccct caaacaagct gtngaatatc tgacttacgg
                                                                        660
 ttcttntggc ccacattttc atnatccacc contentttt aannttantc caaantgt
                                                                        718
```

| <210> 314                 |                  |                                         |                           |            |
|---------------------------|------------------|-----------------------------------------|---------------------------|------------|
| <211> 358                 |                  |                                         |                           |            |
| <211> 330<br><212> DNA    |                  | 4                                       |                           |            |
|                           |                  |                                         |                           |            |
| <213> Homo sapien         |                  |                                         | •                         |            |
| <400> 314                 |                  |                                         |                           |            |
|                           |                  |                                         |                           |            |
| gtttatttac attacagaaa aaa |                  |                                         |                           | - 60       |
| cataatcaaa tatagctgta gta |                  |                                         |                           | 120        |
| caacatgtgt agatctcttg tct |                  |                                         |                           | 180        |
| gctctcggta gtccagccac tgt | gaaacat gctccct  | tta gattaacctc                          | gtggacgctc                | 240        |
| ttgttgtatt gctgaactgt agt |                  |                                         |                           | 300        |
| tctggggcat ttccttgtga tgc | cagaggac caccaca | cag atgacagcaa                          | tctgaatt                  | 358        |
| ·<br>•                    |                  |                                         |                           |            |
| <210> 315                 |                  |                                         |                           |            |
| <211> 341                 |                  |                                         |                           |            |
| <212> DNA                 | 733              |                                         |                           | •.         |
| <213> Homo sapien         |                  | 1.3 + .33:1                             |                           | 1          |
| -                         |                  |                                         |                           |            |
| <400> 315                 | •                | •                                       | the second second         |            |
| taccacctcc ccgctggcac tga | atgageeg cateace | atg gtcaccagca                          | ccatgaagge                | 60         |
| ataggtgatg atgaggacat gga | atogoc cccaago   | ato otctotccaa                          | agaagcgagt                | 120        |
| gaccccatt ctgaagatgt ctg  | gaacete taccage  | agg atgatgatag                          | cccaatgac                 | 180        |
| agtcaccage teceegacca geo | cogatate otectta | aga atcatataga                          | cttcctgaag                | 240        |
| tagettetge tgtaagaggg tgt | tatacca gagacta  | ata caattattaa                          | tectagaett                | 300        |
| gagggggcgg tagatgcagc aca | etaataa acaaata  | ato t                                   | cocagagoec                | 341        |
| gagggggcgg cagacgcagc acc | reggegua geugueg | acy c                                   |                           | J-1.       |
| <210> 316                 |                  | *                                       |                           |            |
| <211> 310<br><211> 151    |                  |                                         |                           |            |
|                           |                  |                                         |                           |            |
| <212> DNA                 | •                |                                         |                           |            |
| <213> Homo sapien         |                  |                                         |                           |            |
| 44005 21.6                |                  |                                         |                           |            |
| <400> 316                 |                  |                                         |                           | <b>C</b> 0 |
| agactgggca agactcttac gco |                  |                                         |                           | 60         |
| tgtgggcctt tctcgagttt ctc |                  | tgg agcgatgtgt                          | tgactggact                | 120        |
| cattcaggga gctctggttg caa | atattagt t       |                                         |                           | 151        |
|                           |                  |                                         | •                         |            |
| <210> 317                 |                  |                                         |                           |            |
| <211> 151                 |                  |                                         |                           |            |
| <212> DNA                 |                  |                                         |                           |            |
| <213> Homo sapien         | •                |                                         |                           |            |
| ·                         |                  | •                                       | .1. 11                    |            |
| <400> 317                 |                  | • • • • • • • • • • • • • • • • • • • • | 1                         |            |
| agaactagtg gatcctaatg aaa | atacctga aacatat | att ggcatttatc                          | aatggctcaa                | 60         |
| atcttcattt atctctggcc tta | accctgg ctcctga  | ggc tgcggccagc                          | agatcccagg                | 120        |
| ccagggctct gttcttgcca cad | cctgcttg a       |                                         |                           | 151        |
|                           |                  |                                         |                           |            |
| <210> 318                 |                  |                                         |                           |            |
| <211> 151                 |                  |                                         |                           |            |
| <212> DNA                 |                  |                                         |                           |            |
| <213> Homo sapien         |                  | ÷                                       |                           |            |
|                           |                  |                                         |                           |            |
| <400> 318                 |                  |                                         | the state of the state of |            |
| actggtggga ggcgctgttt agt | ttaactat tttcaaa | aga atettteaga                          | gggacetect                | 60         |
| gctgcaggct ggagtgtctt tal |                  |                                         |                           | 120        |
| tgggggcggt ttatcaggca gtg | rataaaca t       | and | Socdaddoca                | 151        |
| cygygycygc ccaccaggca gc  | garadaoa c       | . A. *                                  |                           | 101        |
| <210> 319                 |                  |                                         |                           |            |
| <b>ヘムエロン コエフ</b>          |                  | •                                       | •                         |            |

## 1.02

|              | :                | <211>   | 151                 |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           |            |
|--------------|------------------|---------|---------------------|----------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------|------------|
|              |                  | <212>   | DNA                 |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           |            |
|              |                  | <213>   | Homo sapi           | Len                  |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           |            |
|              |                  |         | •                   |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           |            |
|              |                  | <400>   | 319                 |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | •                                                                         |            |
|              | parta            |         |                     | taggtagagt           | atastatasa                                                                                                                                                                                                                      | . attheas                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | acattttcta                                                                |            |
|              | aacta            | gryga ( | cccayaycta          | a cayycacayc         | grgarereag                                                                                                                                                                                                                      | ctttgcaaac                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | acattttcta                                                                | 60         |
|              | catag            | atagt a | actaggtati          | aatagatatg           | taaagaaaga                                                                                                                                                                                                                      | aatcacacca                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | ttaataatgg                                                                | 120        |
| ş            | taaga            | ttggg 1 | tttatgtgat          | tttagtgggt           |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           | 151        |
|              | 1                |         |                     |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Contract to the second                                                    |            |
|              |                  |         | 320 ·               | and the transfer     | 2003 1217                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Programme and the second                                                  |            |
|              |                  | <211>   | 150                 |                      | 11                                                                                                                                                                                                                              | Single State of the Control of the C | 7.                                                                        |            |
|              |                  | <212>   | DNA                 | a present the second | e.                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           | •          |
|              |                  | <213>   | Homo sapi           | en.                  | •                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | ing (1905) in the<br>Caracter of the Caracter<br>Springer of the Caracter |            |
|              |                  |         |                     |                      |                                                                                                                                                                                                                                 | ,                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                           | •          |
|              |                  | <400>   | 330                 |                      |                                                                                                                                                                                                                                 | į                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                           |            |
|              |                  |         |                     |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           |            |
|              | aacta            | gegga t | ceaetagte           | cagtgtggtg           | gaattccatt                                                                                                                                                                                                                      | grgrrggggt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | tctagatcgc                                                                | · 60       |
|              | gagcg            | getge d | ccttttttt           | : tttttttttg         | ggggggaatt                                                                                                                                                                                                                      | ttttttttt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | aatagttatt                                                                | 120        |
|              | gagtg            | ttcta d | cagcttacag          | , taaataccat         |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | an en en en en en en en                                                   | 150        |
|              |                  |         |                     |                      | •                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           |            |
|              | :                | <210>   |                     |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | the stay of                                                               |            |
|              |                  | <211>   | 151                 | 5                    | ara e.                                                                                                                                                                                                                          | f en an                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | . See State of the second                                                 |            |
|              |                  | <212>   | DNA                 |                      |                                                                                                                                                                                                                                 | The state of the s | in and the second                                                         | 1 1 2 2 2  |
|              |                  | <213>   | Homo sapi           | en                   |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | $r_{\mathcal{I}}$                                                         |            |
|              | 1 4 4<br>1 5 5 5 |         |                     |                      |                                                                                                                                                                                                                                 | * * * * * * * * * * * * * * * * * * *                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                           |            |
|              | · · ·            | <400>   | 321                 |                      | e de la companya de<br>La companya de la co | 5 x 1 x 1 + x 2 + 1 + 1 + 1 + 1 + 1 + 1 + 1 + 1 + 1 +                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | jana est. 22 a li d                                                       | 1 14 w 4 t |
|              |                  | ~+++~ + | ttttata             |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | cactgcagtt                                                                |            |
|              | tona             | -cccy ( | tetecacco           | ayyctactt            | aggerragga                                                                                                                                                                                                                      | cttcctctca                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | cactgcagtt                                                                | DE 60      |
|              | Laggg            | iggea t | . Lg taaccag        | ctatggcata           | ggtgttaacc                                                                                                                                                                                                                      | aaaggctgag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | taaacatggg                                                                |            |
|              | tgcct            | ctgag a | aatcaaagt           | cttcatacac           | t .                                                                                                                                                                                                                             | _                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                           | 151        |
|              |                  |         |                     |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           |            |
|              |                  | <210>   |                     |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           |            |
|              |                  | <211>   |                     |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           |            |
|              |                  | <212>   |                     |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           |            |
|              |                  | <213>   | Homo sapi           | en .                 |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           |            |
|              |                  |         |                     |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | •                                                                         |            |
|              |                  | <220>   |                     |                      |                                                                                                                                                                                                                                 | •                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                           | •          |
|              |                  |         | misc feat           | ure                  |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           | • `        |
|              |                  |         | (1)(15              |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | • •                                                                       |            |
|              |                  |         | n = A, T, C         |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | •                                                                         |            |
|              |                  | \223/   | 11 - A, 1, C        | OI G                 |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | ÷                                                                         |            |
|              |                  |         | 200                 | •                    |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | ***                                                                       |            |
|              |                  | <400>   |                     |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           |            |
|              | atccag           | catc t  | tctcctgtt           | tcttgccttc           | ctttttcttc                                                                                                                                                                                                                      | ttcttasatt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | ctgcttgagg                                                                | 60         |
|              | tttggg           | scttg g | tcagtttgc           | cacagggctt           | ggagatggtg                                                                                                                                                                                                                      | acagtcttct                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | ggcattcggc                                                                | 120        |
|              | attgtg           | rcagg g | ctcgcttca           | nacttccagt           | t                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           | 151        |
|              |                  |         |                     |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           |            |
| 2            | - M.:            | <210>   | 323                 |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           |            |
| ~ <u>`</u> - | ****             | <211>   |                     |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           | -          |
|              |                  | <212>   |                     |                      | ,                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | •                                                                         |            |
|              |                  |         | Homo sapi           | en                   | *                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           |            |
|              |                  | \Z_10/  | HOMO Sapt           | 011                  |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | a Contract                                                                |            |
|              |                  | <220>   |                     |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           |            |
|              |                  |         |                     |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           |            |
|              |                  |         | misc_feat           |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | ·                                                                         |            |
|              |                  |         | (1) (15:            |                      |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           |            |
|              |                  | <223>   | $n = \dot{A}, T, C$ | or G                 |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           | •          |
|              |                  |         | :                   |                      |                                                                                                                                                                                                                                 | 1 - 2 - 2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | •                                                                         | •          |
|              |                  | <400>   |                     | •                    |                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           |            |
|              |                  |         |                     | ctttattttt           | aatcctctta                                                                                                                                                                                                                      | ckttqtnaat                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | atattoccta                                                                | 60         |
|              | nagact           | cant ta | actacccag           | tttgtggttt           | twtgggagaa                                                                                                                                                                                                                      | atotaactoo                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | acacttecct                                                                | 120        |
|              | atteaa           | tvaa a  | aagacactt           | ancccatgtg           | u<br>caaaaaaaa                                                                                                                                                                                                                  | geaderay                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | u-ay clayet                                                               |            |
|              | 2                | -2~~ 0  | guvacet             |                      | 9                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                           | 151        |

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                                                                       360
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                                                                                                                                                  10
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20

25

Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly

35

40

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                                                                                                                                                                                                           - 110
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165 170 175
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                                                                 organis (produce) projection in the conference of the conference o
                             <213> Homo, sapien products and ought orders and an about the analysis of the same and an armonional and a same and a sam
                                                                                          ි. පුරුත්තය දුරු ගම්මාවේ සිට ගැන්වීමට කර කම් දුරු ප්රාදේශය දුරුණු දුරුණු දුරුණු දුරුණු දුරුණු දුරුණු දුරුණු ද
මෙහි සිට ගැන්න දුරුණු ගත්තෙන් සිට දුරුණු දුරුණු
මෙහි සිට ගැන්න දුරුණු දුරුණ
      Leu Val Ser Gly Ser Cys Ser Gln Ile Ile Asn Gly Glu Asp Cys Ser
```

|   | 1                                    | ,                              |                                  |                                 | 5                                         |                                  |                       |                                  | •                                       | 10                               |                          |                             | . •                           |                          | 15                            |                                      |             |                              |
|---|--------------------------------------|--------------------------------|----------------------------------|---------------------------------|-------------------------------------------|----------------------------------|-----------------------|----------------------------------|-----------------------------------------|----------------------------------|--------------------------|-----------------------------|-------------------------------|--------------------------|-------------------------------|--------------------------------------|-------------|------------------------------|
|   | Pro                                  | His                            | Ser                              | Gln<br>20                       | Pro                                       | Trp                              | Gln                   | Ala                              | Ala<br>25                               | Leu                              | Val                      | Met                         | Glu                           | Asn<br>30                | Glu                           | Leu .                                |             |                              |
|   | Phe                                  | Cys                            | Ser<br>35                        | Glŷ                             | Val                                       | Leu                              | Val                   | His                              | Pro                                     | Gln                              | Trp                      | Val                         | Leu<br>45                     | Ser                      | Ala                           | Thr                                  |             | ,                            |
|   | His                                  | Cys<br>50                      |                                  | Gln                             | Asn                                       | Ser                              | Tyr<br>55             | Thr                              | Ile                                     | Gly                              | Leu                      | Gly<br>60                   | Leu                           | His                      | Ser                           | Leu                                  |             | ,                            |
|   | Glu<br>65                            |                                | Asp                              | Gln                             | Glu                                       | Pro<br>70                        |                       | Ser                              | Gln                                     | Met                              | Val.                     | Glu                         | Ala                           |                          |                               | s.                                   |             |                              |
| ŧ |                                      |                                |                                  | •                               |                                           | •                                |                       |                                  |                                         |                                  |                          |                             |                               |                          |                               |                                      |             |                              |
|   |                                      | · <:                           | 210>                             | 330                             |                                           | -                                |                       |                                  |                                         |                                  | Ι.                       |                             |                               |                          |                               |                                      |             |                              |
|   |                                      | . <:                           | 211>                             | 70                              |                                           |                                  |                       |                                  |                                         |                                  |                          |                             | ٠., '                         | ١.                       |                               |                                      |             |                              |
|   |                                      | <:                             | 212>                             | DNA                             |                                           |                                  |                       |                                  | 4                                       |                                  |                          |                             |                               |                          |                               |                                      |             | •                            |
|   | *                                    | <u> </u>                       | 213>                             | Homo                            | o saj                                     | pien                             |                       |                                  |                                         | ** .                             | :                        |                             | 1.;                           |                          | :, _                          |                                      | ,           |                              |
|   |                                      |                                |                                  |                                 |                                           |                                  |                       |                                  |                                         |                                  |                          | ٠,،                         |                               |                          |                               |                                      |             |                              |
|   |                                      |                                |                                  | 330                             |                                           |                                  |                       |                                  |                                         | ; .                              |                          |                             |                               | ·.                       |                               | ,                                    |             |                              |
|   |                                      |                                |                                  | tggc                            | ccga                                      | tc c                             | catco                 | cctga                            | ı ct                                    | cege                             | ctc                      | agga                        | atcg                          | ctc.                     | gtct                          | ctggta                               | a           | 60                           |
|   | get                                  | gcag                           | cca                              |                                 |                                           |                                  |                       | , ,                              |                                         |                                  |                          | ٠.                          |                               |                          |                               |                                      | . `         | 70                           |
|   |                                      | _                              | 210>                             | 331                             |                                           | •                                | ٠.                    | •                                |                                         |                                  |                          |                             |                               |                          | • • •                         | ` .                                  | , .         |                              |
|   |                                      | -                              | 211>                             |                                 |                                           |                                  | • '                   |                                  |                                         |                                  |                          |                             |                               |                          |                               |                                      |             |                              |
|   |                                      |                                | 212>                             |                                 |                                           |                                  |                       |                                  |                                         |                                  |                          |                             |                               |                          |                               |                                      | : .         |                              |
|   |                                      |                                |                                  |                                 | o sai                                     | pien                             |                       |                                  |                                         |                                  |                          |                             |                               |                          |                               |                                      |             |                              |
|   |                                      |                                |                                  |                                 |                                           |                                  |                       |                                  |                                         |                                  |                          |                             |                               |                          |                               |                                      |             |                              |
|   | :                                    |                                | 400>                             |                                 |                                           |                                  |                       |                                  |                                         |                                  |                          |                             |                               |                          |                               | 100                                  | . •         |                              |
|   | Gln<br>1                             | His                            | Asn                              | Gly                             | Pro<br>5                                  | Ile                              | Pro                   | Ser                              | Leu                                     | Thr<br>10                        | Pro                      | Pro                         | Ser                           | Gly                      | Ser<br>15                     | Leu                                  |             |                              |
|   | Val                                  | Ser                            | Gly                              | Ser                             | Cys                                       | Ser                              |                       | · *                              | • • • • • • • • • • • • • • • • • • • • |                                  |                          | .:                          |                               | 2                        |                               |                                      |             |                              |
|   | *                                    |                                |                                  | 20                              |                                           |                                  | ` . `                 |                                  | •                                       | ٨                                | ٠.                       |                             |                               | •                        |                               |                                      |             |                              |
|   |                                      |                                |                                  |                                 |                                           | ·                                |                       |                                  |                                         |                                  |                          | · .                         | -                             | ;                        |                               |                                      | ٠.          |                              |
|   |                                      |                                |                                  | 332                             |                                           |                                  | `                     | · .                              |                                         |                                  |                          |                             |                               | <i>.</i>                 |                               |                                      |             |                              |
|   |                                      |                                |                                  | 2507<br>DNA                     |                                           |                                  |                       | _                                |                                         |                                  |                          | • • •                       | •                             |                          |                               |                                      |             |                              |
|   |                                      |                                |                                  |                                 |                                           | pien                             |                       | :                                |                                         |                                  |                          |                             |                               | :                        |                               |                                      |             |                              |
|   |                                      | ~                              |                                  |                                 |                                           | P-1-011                          |                       |                                  |                                         | • • •                            |                          |                             |                               | ; :                      |                               |                                      |             |                              |
|   |                                      |                                | 100>                             |                                 |                                           |                                  |                       |                                  |                                         | at- a a t                        |                          |                             | ~~+~                          |                          |                               | L-a-b-b                              |             | 60                           |
|   |                                      |                                |                                  |                                 |                                           |                                  |                       |                                  |                                         |                                  |                          |                             |                               |                          |                               | tcctto<br>gggtg1                     |             | 60<br>120                    |
|   |                                      |                                |                                  |                                 |                                           |                                  |                       |                                  |                                         |                                  |                          |                             |                               |                          |                               | caggta                               |             | 180                          |
|   |                                      |                                |                                  |                                 |                                           |                                  |                       |                                  |                                         |                                  |                          |                             |                               |                          |                               | cttgc                                |             | 240                          |
|   |                                      |                                |                                  |                                 |                                           |                                  |                       |                                  |                                         |                                  |                          |                             |                               |                          |                               | accago                               |             | 300                          |
|   |                                      |                                |                                  |                                 |                                           |                                  |                       |                                  |                                         |                                  |                          |                             |                               |                          |                               | ctaag                                |             | 360                          |
|   | -                                    |                                | _                                |                                 |                                           |                                  |                       |                                  |                                         |                                  |                          |                             |                               | -                        |                               | tgatgi                               | _           | 420                          |
|   |                                      |                                |                                  |                                 |                                           |                                  |                       |                                  |                                         |                                  |                          |                             |                               |                          |                               | tgggt                                |             | 480                          |
|   |                                      |                                |                                  |                                 |                                           |                                  |                       |                                  |                                         |                                  |                          |                             |                               |                          |                               | ggataq                               |             | 540                          |
|   |                                      |                                |                                  |                                 |                                           |                                  |                       |                                  |                                         |                                  |                          |                             |                               |                          |                               | agggc                                |             | 600                          |
|   |                                      |                                |                                  |                                 |                                           |                                  |                       |                                  |                                         |                                  |                          |                             |                               |                          |                               | tcttca                               |             | 660                          |
|   |                                      |                                |                                  |                                 |                                           |                                  |                       |                                  |                                         |                                  |                          |                             |                               |                          |                               | accct                                |             | 720                          |
|   |                                      |                                |                                  |                                 |                                           |                                  |                       |                                  |                                         |                                  |                          |                             |                               |                          |                               | ggetti                               |             | 780<br>840                   |
|   |                                      |                                |                                  |                                 |                                           |                                  |                       |                                  |                                         |                                  |                          |                             |                               |                          |                               | ccttaa<br>gggtci                     |             | 900                          |
|   |                                      |                                |                                  |                                 |                                           |                                  |                       |                                  |                                         |                                  |                          |                             |                               |                          |                               | acctgo                               |             | 960                          |
|   | ~~~                                  |                                |                                  | 9                               | والانتان                                  | مح مر                            | , cata                |                                  |                                         |                                  |                          |                             |                               | مي د                     | -9-9                          | بوتاتات                              |             |                              |
|   |                                      | recto                          | 2CC - 2                          | atar                            |                                           | aa ca                            | addc:                 | actor                            | CA                                      | attrac                           | acc                      | Caac                        | raga                          | aga.                     | ctac                          | addada                               | a           | 1020                         |
|   | tggg                                 |                                |                                  |                                 | gacta                                     |                                  |                       |                                  |                                         |                                  |                          |                             |                               |                          |                               | agcaga<br>ocacaa                     |             | 1020<br>1080                 |
|   | tggg                                 | acaç                           | gta d                            | cttct                           | gacta                                     | ca aa                            | aatga                 | attct                            | cc                                      | ttcae                            | iggt.                    | tttt                        | caaa                          | acc                      | ttta                          | gcacaa                               | <b>a</b> .  | 1080                         |
|   | tggg<br>ctac<br>agag                 | acaq                           | gta d                            | cttct                           | gacta<br>tgto<br>tccaq                    | ca aa<br>gc cl                   | atga                  | attct<br>ctgct                   | tg                                      | ttcaa<br>gtgto                   | iggt<br>cag              | ttta                        | caaac                         | acc<br>tca               | ttta<br>gtgt:                 | gcacaa<br>actgc                      | 3.<br>C     |                              |
|   | tggg<br>ctac<br>agag<br>agat<br>ctag | acaq<br>jagca<br>tegl<br>jagal | gta d<br>aaa a<br>cct a<br>cat d | ettet<br>acctt<br>aaate<br>ataa | gacta<br>ttgto<br>tccaq<br>gtcto<br>atago | ca aa<br>gc ci<br>gt ca<br>ga ta | atga<br>tgco<br>atgto | attot<br>etget<br>ecaga<br>agaco | tg<br>tt                                | ttcaa<br>gtgtc<br>tactt<br>catat | ggt<br>cag<br>tgc<br>gac | ttta<br>tta:<br>ttci<br>ctg | caaa<br>aaac<br>tgtta<br>caca | acc<br>tca<br>act<br>gct | ttta<br>gtgt:<br>gcca<br>catt | gcacaa<br>actgca<br>gagtta<br>ttccti | a<br>C<br>a | 1080<br>1140<br>1200<br>1260 |
|   | tggg<br>ctac<br>agag<br>agat<br>ctag | acaq<br>jagca<br>tegl<br>jagal | gta d<br>aaa a<br>cct a<br>cat d | ettet<br>acctt<br>aaate<br>ataa | gacta<br>ttgto<br>tccaq<br>gtcto<br>atago | ca aa<br>gc ci<br>gt ca<br>ga ta | atga<br>tgco<br>atgto | attot<br>etget<br>ecaga<br>agaco | tg<br>tt                                | ttcaa<br>gtgtc<br>tactt<br>catat | ggt<br>cag<br>tgc<br>gac | ttta<br>tta:<br>ttci<br>ctg | caaa<br>aaac<br>tgtta<br>caca | acc<br>tca<br>act<br>gct | ttta<br>gtgt:<br>gcca<br>catt | gcacaa<br>actgco<br>gagtta           | a<br>C<br>a | 1080<br>1140<br>1200         |

| gaactagctt. | ctttgttcac | aattcagttc  | ctcccaacca | accagtcttc | acttcaagag | 1380  |
|-------------|------------|-------------|------------|------------|------------|-------|
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| tggaagataa  | tgcacaaaat | gaagggacta  | gttaaggatt | aactagccct | ttaaggatta | 1800  |
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| attatcttag  | ggactgatat | tggtaattat  | ggtcaattta | ataatattt  | ggggcatttc | 2040  |
| cttacattgt  | cttgacaaga | ttaaaatgtc  | tgtgccaaaa | ttttgtattt | tatttggaga | 2100  |
| cttcttatca  | aaagtaatgc | tgccaaagga  | agtctaagga | attagtagtg | ttcccatcac | 2160  |
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| aataaaaacg  | taagaattaa | aagtttgatt  | acaaaaaaa  | a'aaaaaa   |            | 2507  |
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<400> 333 · c

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gagtggcaga gtggtgccaa ccctgttttc ccagtccacg tagacagatt cacagtgcgg

|   | gagiggeaga giggigeeaa |            |                |             |            | 1320    |
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|   | ctatcagaaa cttaaacttg |            |                |             |            | 3000    |
|   |                       |            |                | Cicycaacaa  | ayccagagca |         |
|   | aacaaaaaa aaaaaaaaa   | aaaactcgag | 2000 1 P       | , to the    |            | 3030    |
|   | -010-001              |            | and the second | Martin to a | 4.         |         |
| * | <210> 334             |            | <u>.</u>       |             |            |         |
|   | <211> 2417            |            | · -• ,         |             |            |         |
|   | <212> DNA             |            |                |             |            | و باراد |
|   | <213> Homo sapi       | en         | \$ 1.1 · ·     |             |            |         |
|   |                       |            |                |             |            | •       |
|   | <400> 334             |            |                |             |            |         |
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|   |                       |            |                |             |            |         |

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     ceteacegae etggtgatge tggaeactge gatgaatggt aatgtggatg agaatatgat
                                                                                                                                                                                 2040
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                                                                                                                                                                                 2100
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                                                                                                                                                                                 2160
     acagcctgtc ctgccagctg gatccccagt cccggtcaac cagtaatcaa ggctgagcag
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                                                                                                                                                                                2280
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                                                                                                                                                                            2340
    ctgtctacat ctataatcac tatgcatact agtctttgtt agtgtttcta ttcmacttaa
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                                                                                                                                                                                 2417
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<211> 2984

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                   400> 335 First State (1995) Silen 2014 A Republication of the control of the c
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    aaaacactte aggegeeett ceaaggette eccaaacee taaggageeg cagaageget
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    getgtataaa cagaacteca etgcaagagg gggggeeggg ceaggagaat eteegettgt
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                                                                                                                                                                               1800
                                                                                                                                                                               1860
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                                                                                                                                                                               1980
                                                                                                                                                                               2040
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                                                                    2580
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                                                                    2640
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                                                                    27.60
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Pro Lys Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln
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Val Ile Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala
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Pro Glu Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln
Val Lys Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln
                85
                                   90
Leu Ser Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala
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Leu Lys Glu Glu Ala Phe Ser Arg Ala Ser Leu Val Ser Val Tyr Asn
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Ser Tyr Pro Tyr Tyr Pro Tyr Leu Tyr Cys Val Gly Ser Trp Ser Pro
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360

420

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cettcaattt tetetttggc tgacgacgga gteegtggtg teeegatgta actgacecet

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| ctg                    |             |            |                                       |                    | 483 |
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| tatttttact aaccattcta  | tttttataga  | aatagctgag | agtttctaaa                            | ccaactctct         | 120 |
| gctgccttac aagtattaaa  |             |            |                                       |                    | 180 |
| attaatttaa taatttctga  |             |            |                                       |                    | 240 |
| aatttactta atgaaaaact  |             |            |                                       | ttaagtactc         | 300 |
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| <210> 542<br><211> 592 |             |            |                                       |                    |     |
| <211> 552<br><212> DNA | •           |            |                                       |                    |     |
| <213> Homo sapie       | an          |            |                                       |                    |     |
| 1220 Home Dupa         | <b></b>     | ·          | ,                                     |                    |     |
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| caatgtggaa acttcttata  |             |            |                                       |                    | 120 |
| cctggcaggt aaaccaatgc  | caagagagtg  | atggaaacca | ttggcaagac                            | tttgttgatg         | 180 |
| accaggattg gaattttata  |             |            |                                       |                    | 240 |
| tecetcagaa gagtgtaaag  |             |            |                                       |                    | 300 |
| aagtgccact gtggaaagag  |             |            |                                       |                    | 360 |
| tcagcatggg ctgtttggtg  |             |            |                                       |                    | 420 |
| cccgtgtcct tatgcaaata  |             |            |                                       |                    | 480 |
| agttcttctt ggtttgtgat  |             |            |                                       |                    | 540 |
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| <211> 382              |             | •          |                                       |                    |     |
| <212> DNA              |             |            |                                       | :                  |     |
| <213> Homo sapie       | en          |            |                                       | * *                |     |
| •                      |             |            | 1,9                                   |                    |     |
| <400> 343              |             |            |                                       |                    |     |
| ttettgacet ceteeteett  | caagctcaaa  | caccacctcc | cttattcagg                            | accggcactt         | 60  |
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| cttgtaactc tcctttctcc  |             | _          | _                                     | <b>.</b>           | 180 |
| agacttcttg attgtcagtc  |             |            |                                       |                    | 240 |
| ctgactgccc aaggggctca  | gaaccccagc  | aatcccttcc | tttcactacc                            | ttcttttttg         | 300 |
| ggggtagttg gaagggactg  | aaattgtggg  | gggaaggcag | gaggcacacc                            | aataaagagg         | 360 |
| aaaccaccaa gctgaaaaaa  | aa          |            |                                       |                    | 382 |
| <210> 344              |             |            | , , , , , ,                           | gradicione albumpe |     |
| <211> 536              | •           |            | · · · · · · · · · · · · · · · · · · · |                    | · 3 |
| <212> DNA              |             |            |                                       |                    |     |
| <213> Homo sapie       | en          |            |                                       |                    |     |
| ·                      |             |            |                                       |                    |     |
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| gtttaggggg atgccaagga  |             |            |                                       |                    | 180 |
| agtctttcag agaaatggat  |             |            |                                       |                    | 240 |
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|                                                                                                                                            | atttgatcta<br>gccactaata<br>tgagtgacta                                                                                                                              | gaaattgccc<br>gttatgtcat                             | tccttttacc                                            | cctaccatga<br>aatcatcatc                             | ctagccctaa                                           | 360<br>420<br>480<br>536 |
|--------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------|-------------------------------------------------------|------------------------------------------------------|------------------------------------------------------|--------------------------|
| <210<br><211<br><212                                                                                                                       | > 345<br>> 251<br>> DNA<br>> Homo sapie                                                                                                                             |                                                      | <i>J J J</i>                                          | •                                                    | \$ 5 + 12 to<br>\$ 7 \$ 22<br>2 5 \$ 25<br>2 5 \$ 25 |                          |
| <400<br>accttttgag<br>tgaatgaagc<br>gcgtgggcca                                                                                             | > 345<br>gtctctctca<br>ccccatcttt<br>ggaaatcaca<br>tcggatttgg                                                                                                       | ccacctccac<br>gtgcctcctg<br>tcctacactg               | agccaccgtc<br>aaaagagagt<br>cccaggagcc                | accgtgggat<br>ggaagtgtcc<br>agacacattt               | gtgctggatg<br>gaggactttg<br>atggaacaga<br>ccggacactg | 60<br>120<br>180         |
| <211<br><212                                                                                                                               | > 346<br>> 282<br>> DNA<br>> Homo sapie                                                                                                                             | en                                                   |                                                       |                                                      |                                                      | ·                        |
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| ggccccacte                                                                                                                                 | cccaaggcgc                                                                                                                                                          | <del>-</del>                                         |                                                       |                                                      |                                                      |                          |
| <210:<br><211:<br>· <212:                                                                                                                  | > 347<br>> 201<br>> DNA<br>> Homo sapie                                                                                                                             |                                                      |                                                       |                                                      |                                                      |                          |
| <210: <211: <212: <213: <220: <221: <222: <223: <400: acacacataa taaatataac tctgagactg                                                     | > 347 > 201 > DNA > Homo sapie > misc_featu > (1) (201 > n = A,T,C > 347 tattataaaa ttttaaaana                                                                      | re<br>or G<br>tgccatctaa<br>ntactancag<br>cccagaccca | ttggaaggag<br>cttttaccta                              | ctttctatca<br>ngctcctaaa                             | ttgcaagtca<br>tgcttgtaaa<br>atatcatctt               | 60<br>120<br>180<br>201  |
| <210: <211: <212: <213: <220: <221: <222: <223: <400: acacacataa taaatataac tctgagactg tataaagaat <210: <211: <212: <213: <400: ctgttaatca | > 347 > 201 > DNA > Homo sapie > misc_featu > (1) (201 > n = A,T,C > 347 tattataaaa ttttaaaana actggaccca tttttttgt > 348 > 251 > DNA > Homo sapie > 348 caacatttgt | re  or G  tgccatctaa ntactancag cccagaccca c         | ttggaaggag<br>cttttaccta<br>gggcaaagat                | ctttctatca ngctcctaaa acatgttacc                     | ttgcaagtca<br>tgcttgtaaa<br>atatcatctt               | 60<br>120<br>180<br>201  |

| aggagacact cccagcatgg<br>ggggaaggtt ttattataga<br>gccctgcctc c |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 180<br>240<br>251                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|----------------------------------------------------------------|--------------------------|--------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
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| <213> Homo sapi                                                | en ,                     | •                  | •                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | • .                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <400> 349 taaaaatcaa gccatttaat                                | totatottto               | aaqqtaaaca'        | atatatagga                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | gctggatcac             | 60                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| aacccctgag gatgccagag                                          |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 120                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| cagaagggtc tgaactctac                                          |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 180                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
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| actectggtt t                                                   |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 251                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| L                                                              | <u> </u>                 |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | •                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| <210> 350                                                      |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <211> 908                                                      |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <212> DNA                                                      |                          |                    | e in the second of the second |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <213> Homo sapi                                                | en                       |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| В                                                              |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 4.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| <400> 350                                                      |                          |                    | ,                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| ctggacactt tgcgagggct                                          |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 60                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| agcccgcccg gtgaagctcg                                          |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 120                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| cggctggaat tgctctggtt                                          |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 180                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| cacctgtaaa tttgatgggg                                          |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 240                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| gttcaagtgc aacaatgact                                          |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 300                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| tgagtgttac ctgcgacagg                                          |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 360                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| aggatcatgt gccacagtcc                                          |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 420                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| ctgtgatatt tgccagtttg                                          |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 480<br>540                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| gtgtaatatt gactgttctc ttatgataat gcatgccaaa                    |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 600                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| catgtctttg ggtcgatgtc                                          |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 660                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| ttatgcaaga acagattatg                                          |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 720                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| ccacatacct tgtccggaac                                          |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 780                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| tatcaatatg caggagccat                                          |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 840                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| aaaaaaggac tacagtgttc                                          |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 900                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| aatcgcag                                                       |                          | 5505535000         | gonoguocuo                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | aguadgeoec             | 908                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|                                                                | • •                      |                    | • • •                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <210> 351                                                      |                          | Jan Arthur Barrier |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <211> 472                                                      | •                        |                    | •                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                        | in the state of th |
| <212> DNA                                                      |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | A Tillian and a second | e e de de la companya de la company<br>La companya de la co                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| <213> Homo sapie                                               | en                       |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| _                                                              |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | N 1 / 10               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
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| ccagttattt gcaagtggta                                          | agagcctatt               | taccataaat         | aatactaaga                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | accaactcaa             | 60                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| gtcaaacctt aatgccattg                                          |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| cattaacttg attttaaaat                                          |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 180                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| tatgataaaa acaaccattg                                          |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 240                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| atatatcctt cgacatcaat                                          |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 300                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| gatctgtcca caacaaactt                                          |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 360                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| tcagcccct tttggcctgt                                           |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | 420                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| gtaatatata tttagggaag                                          | atgttgcttt               | gcccacacac         | gaagcaaagt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | aa                     | 472                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|                                                                |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        | . 11                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| <210> 352                                                      |                          |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | •                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <211> 251                                                      |                          |                    | in rheigh i                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <212> DNA                                                      | A Company of the Company |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <213> Homo sapie                                               | en                       |                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | •                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |

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<400> 352
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                                                                    .120
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                                                                    360
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                                                                    540
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                                                                    660
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                                                                    420
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| tcatctgcaa aataggtcta ggatttct                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | tc caaccatttc atgagttgtg aagctaaggc 480                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | at gcagaaagcc tttctggctt tcttatctgt 540                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | aca tgatcaagtc aatgagtaaa attttaaggg 600                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| attagatttt cttgacttgt atgtatct                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | gt gagatettga ataagtgace tgacatetet 660                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| gcttaaagaa aaccag "                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 676                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| J                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| 2010× 250                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <210> 356                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <211> 574                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <212> DNA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <213> Homo sapien                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| ZID HOMO Sapien                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <400> 356                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | and the state of t |
| ttttttttt tttttcagga aaacatto                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | tc ttactttatt tgcatctcag caaaggttct 60                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| catotogoac ctoactogoa toaaacca                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | aa gttcgtaggc caacaaagat gggccactca 120                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | cet atgagtatet gacacetgtt cetetettea 180                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| gtctcttagg gaggcttaaa tctgtcto                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | cag gtgtgctaag agtgccagcc caaggkggtc : 240                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| aaaagtccac aaaactgcag tetttgct                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | gg gatagtaagc caagcagtgc ctggacagca 300                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| andtattt attaggene nastang                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | eag acaggactet aatcgtgete ttattcaaca 360                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| the black of the base of the b | ay acayyactor aaccycycec crarceaca 500                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | aaa aagccaatct ctctcgtggc acagggaagg 420                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | atc taacaaaggc atctaccgaa gtctggtctg 480                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| gatagacggc acagggagct cttaggto                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | cag cgctgctggt tggaggacat tcctgagtcc 540                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| agetttgeag cetttgtgea acagtact                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| agocceguag cocceguaca acageac                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
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| <211> 393                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 1. 19 1. 有身上的一点,有人的一点,一点,一点的一点的一点。                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| <212> DNA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
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| <213> Homo sapien                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| the state of the s |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <400> 357                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | •                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
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| taatatggkg kcttgttcac tatactta                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | aa aatgcaccac tcataaatat ttaattcagc 120                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| taatatggkg kettgtteae tataetta aageeacaae caaraettga ttttatea                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | aa aatgcaccac tcataaatat ttaattcagc 120 ac aaaaacccct aaatataaac ggsaaaaaag 180                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| taatatggkg kettgtteae tataetta aageeacaae caaraettga ttttatea                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | aa aatgcaccac tcataaatat ttaattcagc 120                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| taatatggkg kettgtteae tataetta<br>aageeacaae caaraettga ttttatea<br>atagatataa ttatteeagt ttttttaa                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | haa aatgcaccac tcataaatat ttaattcagc 120<br>hac aaaaacccct aaatataaac ggsaaaaaaag 180<br>haa cttaaaarat attccattgc cgaattaara 240                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| taatatggkg kettgtteae tataetta<br>aageeacaae caaraettga tittatea<br>atagatataa ttatteeagt tittttaa<br>araarataag tgttatatgg aaagaagg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | haa aatgcaccac tcataaatat ttaattcagc 120<br>hac aaaaacccct aaatataaac ggsaaaaaag 180<br>haa cttaaaarat attccattgc cgaattaara 240<br>hgc attcaagcac actaaaraa cctgaggkaa 300                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| taatatggkg kettgtteae tataetta<br>aageeacaae caaraettga tittatea<br>atagatataa ttatteeagt tittttaa<br>araarataag tgttatatgg aaagaagg<br>gcataatetg tacaaaatta aactgtee                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | haa aatgcaccac tcataaatat ttaattcagc 120 hac aaaaacccct aaatataaac ggsaaaaaag 180 haa cttaaaarat attccattgc cgaattaara 240 hgc attcaagcac actaaaraaa cctgaggkaa 300 htt tttggcattt taacaaattt gcaacgktct 360                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| taatatggkg kettgtteae tataetta<br>aageeacaae caaraettga tittatea<br>atagatataa ttatteeagt tittttaa<br>araarataag tgttatatgg aaagaagg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | haa aatgcaccac tcataaatat ttaattcagc 120 hac aaaaacccct aaatataaac ggsaaaaaag 180 haa cttaaaarat attccattgc cgaattaara 240 hgc attcaagcac actaaaraaa cctgaggkaa 300 htt tttggcattt taacaaattt gcaacgktct 360                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| taatatggkg kettgtteae tataetta<br>aageeacaae caaraettga tittatea<br>atagatataa ttatteeagt tittttaa<br>araarataag tgttatatgg aaagaagg<br>gcataatetg tacaaaatta aactgtee                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | haa aatgcaccac tcataaatat ttaattcagc 120 hac aaaaacccct aaatataaac ggsaaaaaag 180 haa cttaaaarat attccattgc cgaattaara 240 hgc attcaagcac actaaaraaa cctgaggkaa 300 htt tttggcattt taacaaattt gcaacgktct 360                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| taatatggkg kettgtteae tataetta<br>aagecacae caaraettga ttttatea<br>atagatataa ttatteeagt ttttttaa<br>araarataag tgttatatgg aaagaagg<br>gcataatetg tacaaaatta aactgtee<br>ttttttett tttetgtttt ttttttt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | haa aatgcaccac tcataaatat ttaattcagc 120 hac aaaaacccct aaatataaac ggsaaaaaag 180 haa cttaaaarat attccattgc cgaattaara 240 hgc attcaagcac actaaaraaa cctgaggkaa 300 htt tttggcattt taacaaattt gcaacgktct 360                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| taatatggkg kettgtteae tataetta aageeacaae caaraettga ttttatea atagatataa ttatteeagt ttttttaa araarataag tgttatatgg aaagaagg gcataatetg tacaaaatta aactgtee ttttttett tttetgtttt ttttttt <210> 358                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | haa aatgcaccac tcataaatat ttaattcagc 120 hac aaaaacccct aaatataaac ggsaaaaaag 180 haa cttaaaarat attccattgc cgaattaara 240 hgc attcaagcac actaaaraaa cctgaggkaa 300 htt tttggcattt taacaaattt gcaacgktct 360                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| taatatggkg kettgtteae tataetta aageeacaae caaraettga tittatea atagatataa tiatteeagt titttataa araarataag tgttatatgg aaagaagg geataatetg tacaaaatta aactgtee tittitett tittetgttit tittitit  <210> 358 <211> 630                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | haa aatgcaccac tcataaatat ttaattcagc 120 hac aaaaacccct aaatataaac ggsaaaaaag 180 haa cttaaaarat attccattgc cgaattaara 240 hgc attcaagcac actaaaraaa cctgaggkaa 300 htt tttggcattt taacaaattt gcaacgktct 360                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| taatatggkg kettgtteae tataetta aageeacaae caaraettga tittatea atagatataa tiatteeagt tittitaa araarataag tgttatatgg aaagaagg gcataatetg tacaaaatta aactgtee tittitett tittetgttit tittitit  <210> 358 <211> 630 <212> DNA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | haa aatgcaccac tcataaatat ttaattcagc 120 hac aaaaacccct aaatataaac ggsaaaaaag 180 haa cttaaaarat attccattgc cgaattaara 240 hgc attcaagcac actaaaraaa cctgaggkaa 300 htt tttggcattt taacaaattt gcaacgktct 360                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| taatatggkg kettgtteae tataetta aageeacaae caaraettga tittatea atagatataa tiatteeagt titttataa araarataag tgttatatgg aaagaagg geataatetg tacaaaatta aactgtee tittitett tittetgttit tittitit  <210> 358 <211> 630                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | haa aatgcaccac tcataaatat ttaattcagc 120 hac aaaaacccct aaatataaac ggsaaaaaag 180 haa cttaaaarat attccattgc cgaattaara 240 hgc attcaagcac actaaaraaa cctgaggkaa 300 htt tttggcattt taacaaattt gcaacgktct 360                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| taatatggkg kettgtteae tataetta aageeacaae caaraettga tittatea atagatataa tiatteeagt tittitaa araarataag tgttatatgg aaagaagg gcataatetg tacaaaatta aactgtee tittitett tittetgttit tittitit  <210> 358 <211> 630 <212> DNA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | haa aatgcaccac tcataaatat ttaattcagc 120 hac aaaaacccct aaatataaac ggsaaaaaag 180 haa cttaaaarat attccattgc cgaattaara 240 hgc attcaagcac actaaaraaa cctgaggkaa 300 htt tttggcattt taacaaattt gcaacgktct 360                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| taatatggkg kettgtteae tataetta aageeacaae caaraettga tittatea atagatataa ttatteeagt titttaa araarataag tgttatatgg aaagaagg gcataatetg tacaaaatta aactgtee ttttttett tttetgttt tittttt  <210> 358                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | haa aatgcaccac tcataaatat ttaattcagc 120 hac aaaaacccct aaatataaac ggsaaaaaag 180 haa cttaaaarat attccattgc cgaattaara 240 hgc attcaagcac actaaaraaa cctgaggkaa 300 htt tttggcattt taacaaattt gcaacgktct 360                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| taatatggkg kettgtteae tataetta aageeacaae caaraettga tittatea atagatataa ttatteeagt tittttaa araarataag tgttatatgg aaagaagg gcataatetg tacaaaatta aactgtee ttttttett tttetgttt tittttt  <210> 358 <211> 630 <212> DNA <213> Homo sapien  <400> 358                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | taa aatgcaccac tcataaatat ttaattcagc 120 tac aaaaacccct aaatataaac ggsaaaaaag 180 taa cttaaaarat attccattgc cgaattaara 240 tagc attcaagcac actaaaraaa cctgaggkaa 300 tt tttggcattt taacaaattt gcaacgktct 360 tt tac 393                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| taatatggkg kettgtteae tataetta aageeacaae caaraettga tittatea atagatataa ttatteeagt titttaa araarataag tgttatatgg aaagaagg geataatetg tacaaaatta aactgtee titttett tittetgttit tittitit  <210> 358 <211> 630 <212> DNA <213> Homo sapien  <400> 358 acagggtaaa caggaggate ettgetet                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | taa aatgcaccac tcataaatat ttaattcagc laac aaaaacccct aaatataaac ggsaaaaaag laac cttaaaarat attccattgc cgaattaara lagc attcaagcac actaaaraaa cctgaggkaa set tttggcattt taacaaattt gcaacgktct set tac 300 393 300 300 300 300 300 300 300 300                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| taatatggkg kettgtteae tataetta aageeacaae caaraettga tittatea atagatataa ttatteeagt titttata araarataag tgttatatgg aaagaagg gcataatetg tacaaaatta aactgtee ttttttett tttetgttt tittttt  <210> 358 <211> 630 <212> DNA <213> Homo sapien  <400> 358 acagggtaaa caggaggate ettgetet ttaatgttta taggaaaatg atgagttt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | taa aatgcaccac tcataaatat ttaattcagc 120 tac aaaaacccct aaatataaac ggsaaaaaag 180 taa cttaaaarat attccattgc cgaattaara 240 tagc attcaagcac actaaaraaa cctgaggkaa 300 tt tttggcattt taacaaattt gcaacgktct 360 tt tac 393  tca cggagcttac attctagcag gaggacaata 60 tat gacaaaggaa gtagatagtg ttttacaaga 120                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| taatatggkg kettgtteae tataetta aageeacaae caaraettga tittatea atagatataa ttatteeagt titttata araarataag tgttatatgg aaagaagg gcataatetg tacaaaatta aactgtee ttttttett tttetgttt tittttt  <210> 358 <211> 630 <212> DNA <213> Homo sapien  <400> 358 acagggtaaa caggaggate ettgetet ttaatgttta taggaaaatg atgagttt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | taa aatgcaccac tcataaatat ttaattcagc laac aaaaacccct aaatataaac ggsaaaaaag laac cttaaaarat attccattgc cgaattaara lagc attcaagcac actaaaraaa cctgaggkaa set tttggcattt taacaaattt gcaacgktct set tac 300 393 300 300 300 300 300 300 300 300                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
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| taatatggkg kettgtteae tataetta aageeacaae caaraettga tittatea atagatataa ttatteeagt titttata araarataag tgttatatgg aaagaagg gcataatetg tacaaaatta aactgtee tittttett tittetgttit tittitit  <210> 358 <211> 630 <212> DNA <213> Homo sapien  <400> 358 acagggtaaa caggaggate ettgetet ttaatgtta taggaaaatg atgagttt gcatagagta gggaagetaa tecageac gagtttaaae tgagagaage aagtgett                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | taa aatgcaccac tcataaatat ttaattcagc 120 aac aaaaacccct aaatataaac ggsaaaaaag 180 aac cttaaaarat attccattgc cgaattaara 240 ggc attcaagcac actaaaraaa cctgaggkaa 300 att tttggcattt taacaaattt gcaacgktct 360 att tac 393 accaaggaa gtagatagtg ttttacaaga 120 aag ggaggtcaca gagacatccc taaggaagtg 180 aa actgaaggat gtgttgaaga agaagggaga 240                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
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|------------|------------|---------------------------------------|------------|------------|------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
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|            |            |                                       |            | tgggcgcttc |            | 480                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
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Control of the Contro

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                                                                         960
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 accagaaata aataa
                       សាសន៍ប្រាស់ សេសស៊ីនិតន បច្ចេក្សាសាសសាសព្វថា ១០១៦ សេសមាធ
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                                                   The second of th
Leu Asp Gly Gln Gly Glu Arg Gln Glu Gln Arg Gly His Phe Trp Arg
                                                   Pro Gln Arg Leu Leu Cys Glu Asp Ala Trp Glu Gln Glu Val Gln Val
                                                   70
                                                                                                   75 . 80
Val Leu Pro Leu Pro Leu Leu Gln Gly Ser Gly Lys Ser Asn Val
                                                                                           90
                                                                                                          95
                                        85
Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr
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                                                                                105
                                                                                                                                    110
His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp
             115
                                                                     120
Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp:
ug 130 - 44 - 2, 1444 yeg 135 mg g 1 mg/g tha 140 gram dang fitter
Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser
145 grada japon 150 grada i japon 155 minimaga ng na 4 160 da 7
Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Cys
               \sim 1.00 
m (165) 
m (175) 
m (175) 
m (170) 
m (170) 
m (170) 
m (170)
Gin Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala
  age and the specific state of the specific o
Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly
 And 195 : 200 : 200 : 300 : 300 : 205 : 100 : 205
Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr
 may, 210 January and Proceedings 215 section of the contract of 220 to the contract of the
Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Tyr
               235 galasta harakan 240 km a ki
Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu
245 250
Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys
  Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu
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260 265 270

Leu Thr Pro Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
275 280 285

Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn

Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys

Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly

220

235

215

245 250

230

| Lys        | Phe<br>290 |                         | Ile        | Lys        | 'Lys        | Lys<br>295 |            | Asn        | Leu         | Asn         | Ala<br>300 |              | Asp         | Arg          | Tyr        |
|------------|------------|-------------------------|------------|------------|-------------|------------|------------|------------|-------------|-------------|------------|--------------|-------------|--------------|------------|
| Gly<br>305 | Arg        | Thr                     | Ala        |            | Ile<br>'310 | Leu        | Ala        | ۷al        | Суз         | Cys<br>315  |            | Ser          | Ala         | Ser          | Ile<br>320 |
| Val        | Ser        | Leu                     | Leu        | Leu<br>325 | Glu         | Gln        |            | Ile        | Asp<br>'330 |             | Ser        | Ser          | Gln         | Asp<br>335   |            |
| Ser        | Gly        | Gln                     | Thr<br>340 |            | Arg         |            | Tyr        |            |             | _           | Ser        | His          |             |              | Val        |
| Ile        | Суз        | Gln<br>355              |            | Leu        | Ser         | Asp        | Tyr<br>360 | Lys        | Glu         | Lys         | Gln        | Met<br>. 365 | Leu         | Lys          | Ile        |
| Ser        | Ser<br>370 | Glu                     | Asn        | Ser        | Asn         |            | Glu        | Asn        | Val         | Ser         | Arg        | Thr          | Arg         | Asn          | Lys        |
| Pro<br>385 |            | Thr                     |            |            | Val<br>390  | Val        |            |            | Asp         | Ser         | 380<br>Met | Pro          | Ala         | Ala          | Ser        |
|            | Val        | Lys                     | Lys        | Pro        | Phe         |            |            | Arg        | Ser<br>410  |             | Met        | Gly          | Lys         |              |            |
| Cys        | Arg        | Cys                     | Phe        | Pro        |             | Суз        | Arg        | Glu<br>425 |             | Gly         | Lys        | Ser          | Asn<br>430  | Val          | Gly        |
| Thr        | Ser        | Gly<br>435              |            | His        | Asp         | 'Asp       | Ser<br>440 |            | Met         | Lys         | Thr        |              | Arg         |              | Lys        |
| Met        | Gly<br>450 | Lys                     | Trp        | Cys        | Arg         | His<br>455 | Cys        | Phe        | Pro         | Суз         | Cys<br>460 |              |             |              |            |
| Lys<br>465 | Ser        | Asn                     | Val        | .Gly       | Ala<br>470  | Ser        | :Gly       | 'Asp       | His         | Asp<br>475  | Asp        | Ser          | Ala         | Met          | Lys<br>480 |
| •          |            |                         |            | 485        |             | _          | _          | _          | 490         |             |            | _            |             | 495          | 50 ·       |
|            |            |                         | 500        |            | Lys         |            |            | 505        |             |             | 7.3        |              | 510         |              | _          |
|            |            | 515                     |            |            |             |            | 520        | -          |             |             |            | 525          |             | _            | ·Leu       |
|            | 530        |                         | <i>‡</i>   |            | Ala         | 535        |            |            | _           | _           | 540        |              | ٠,          | _            | _          |
| 545        |            |                         |            | 3.5        | Arg<br>550  | ı          |            |            | ··^         | 555         | t          |              |             | •            | 560        |
|            |            |                         |            | 565        |             |            |            |            | 570         | Ĵ           | _          |              |             | <b>575</b> . | ė,         |
|            | _          |                         | 580        |            | Asp         |            | _          | 585        |             |             |            |              | 590         | •            | •          |
|            |            | 595                     |            |            | Leu         | ,          | 600        |            |             |             | -          | 605          |             | •            |            |
|            | 610        |                         | 3.         |            | Leu .       | 615        |            | ·          |             |             | 620        | ī            | Ţ           |              | _          |
| 625        | Tyr        | GTA                     |            | Thr        | Thr 630     | /Leu       | His        | Tyr        |             | 11e         | Tyr        | Asn          | Glu         | Asp          | Lys 640    |
| Leu        | Met        | Ala                     | Lys        | Ala<br>645 | Leu         | Leu        | Leu        | Tyr        | Gly<br>650  |             | Asp        | Ile          | Glu.        |              | Lys        |
| Asn        | Lys        | His                     | Gly<br>660 | Leu        | Thr         | Pro        | Leu        | Leu<br>665 | Leu         | Gly         | Val        | His          | Glu:<br>670 |              |            |
| Gln        | Gln        | Val <sup>.</sup><br>675 | Val        | Lys        | Phe         |            | Ile<br>680 | Ľys        | Lys         | Lys         |            | Asn<br>685   | Leu         | Asn:         | Ala        |
|            | 690        |                         | i-         |            |             | 695        | ζ';        | : 3        |             |             | 700        | 5            | : 2         |              | _          |
| Ser<br>705 | Ala        | Ser                     | Ile        | Val        | Ser:        | Leu        |            |            | Glu         | Gln.<br>715 | Asn:       | Ile:         |             | Val          | Ser<br>720 |
|            | Gln        | qzA                     | Leu        | Ser: 725   | Gly.        |            |            |            |             | Glu         | Tyr        | Ala          |             |              | Sîr        |
| His        | His        | Hís                     | Val<br>740 |            |             |            | Leu        | Leu<br>745 |             | Asp.        | Tyr        | Lys          | G1u<br>750  |              | Gln        |

|     |             |             |                         |             |             |             |             |             |            |             | -          |             |            |            |             |             |     |              |     |
|-----|-------------|-------------|-------------------------|-------------|-------------|-------------|-------------|-------------|------------|-------------|------------|-------------|------------|------------|-------------|-------------|-----|--------------|-----|
|     | Met-        | Leu         | Lys <sup>-</sup><br>755 | -I-1        | Ser         | Ser         | Glu         | Asn<br>760  | Ser        | Asn         | Pro        | Glu         | Gln<br>765 | Asp        | Leu         | Lys         |     |              |     |
|     | Leu         | Thr<br>770  |                         | Glu         | Glu         | Glu         | Ser<br>775  | -           | Arg        | Phe         | Lys        | Gly<br>780  | Ser        | Glu        | Asn         | Ser         |     | ٠.           |     |
| 1 ( | Gln         |             | Glu                     | Lvs         | Met         | Ser         |             | Glu         | Pro        | Glu         | Ile        |             | Lys        | Asp        | Gly         | Asp         |     | J.S.         |     |
|     | 785         |             |                         | _           |             | 790         |             |             |            |             | 795        |             |            |            |             | 800         |     |              |     |
| •   | Arg         | Glu         | Val                     | Glu         | Glu<br>805  | Glu         | Met         | Lys         | Lys        | His<br>810  | Glu        | Ser         | Asn        | Asn        | Val<br>815  | Gly         | ·   |              |     |
|     | Leu         | Leu         | Glu                     | Asn<br>820  | Leu         | Thr         | Asn         | Gly         | Val<br>825 |             | Ala        | Gly         | Asn        | Gly<br>830 | Asp         | Asn         | ,   | ٠.           |     |
| ' ( | GLy         | Leu         | Ile<br>835              | Pro         | Gln         | Arg         | Lys         | Ser<br>840  | _          | Thr         | Pro        | Glu         | Asn<br>845 | Gln        | Gln         | Phe         |     | ė            | •   |
|     | Pro         | Asp<br>850  |                         | Glu         | Ser         |             | Glu<br>855  | Tyr         | His        | Arg         | Ile        | Cys<br>860  | Glu        | Leu        | Val         | Ser         | -   |              |     |
|     | Asp<br>865  |             | Lys                     | Glu         | Lys         |             |             | Pro         | Lys        | Tyr         | Ser<br>875 | Ser         | Glu        | Asn        | Ser         | Asn<br>880  |     |              |     |
|     |             | Glu         | Gln                     | Asp.        | Leu<br>885  |             | Leu         | Thr         | Ser        | Glu<br>890  |            | Glu         | Ser        | Gln        | Arg<br>895  |             |     |              |     |
| •   | Glu         | Gly         | Ser                     | Glu<br>900  | _           | Gly         | Gln         | Pro         | Glu<br>905 | Leu         | Ģlu        | Asn         | Phe        | Met<br>910 | Ala         | Ile         |     | •,•*         |     |
| 1   | Glu         | Glu         | Met                     |             | Lys         | His         | Gly         | Ser<br>920  | Thr        | His         | Val        | Gly         | Phe<br>925 | Pro        | Glu         | Asn         |     |              |     |
| • ; | Leu         | Thr<br>930  | Asn                     | Gly         | Ala         | Thr         | Ala<br>935  | Gly         | Asn        | Gly         | Asp        | Asp<br>940  | Gly        | Leu        | Ile         | Pro         |     | . •          |     |
|     | Pro<br>945  |             | Lys                     | Ser         | Arg         | Thr<br>950  |             | Glu         | Ser        | Gln         | Gln<br>955 | Phe         | Pro        | Asp        | Thr         | Glu<br>960  | · · | ÷            |     |
|     |             | Glu         | Glu                     | Tyr         | His<br>965  |             | Asp         | Glu         | Gln        | Asn<br>970  | Asp        | Thr         | Gln        | Гуз        | Gln<br>975  | Phe         | :   | , ,          |     |
|     | Суз         | Glu         | Glu                     | Gln<br>980  | Asn         | Thr         | Gly         | Ile         | Leu<br>985 |             | Asp        | Glu         | Ile        | Leu<br>990 | Ile         | His .       |     |              |     |
| •   | Glu         | Glu         | Lys<br>995              | Gln         | Ile         | Glu         | Val         | Val<br>1000 |            | Lys         | Met        | Asn         | Ser<br>100 |            | Leu         | Ser         |     | •.           |     |
|     | Leu         | Ser<br>1010 | _                       | Lys         | Lys         | Glu         | Lys<br>1019 |             | Ile        | Leu         |            | Glu<br>1020 |            | Ser        | Thr         | Leu         |     |              |     |
|     | Arg<br>1025 |             | Glu                     | Ile         | Ala         | Met<br>1030 |             | Arg         | Leu        | Glu         | Leu<br>103 | _           | Thr        | Met ·      | Lys         | His<br>1040 |     | ٠,           | •   |
|     | Gln         | Ser         | Gln                     | Leu         | Pro<br>1045 |             | Thr         | His         | Met        | Val<br>1050 |            | Glu         | Val        | Asp        | Ser<br>1055 |             | .•  |              |     |
|     | Pro         | Ala         | Ala                     | Ser<br>1060 |             | Val         | Lys         | Lys         | Pro<br>106 |             | Gly        | Leu         | Arg        | Ser<br>107 | Lys<br>0    | Met         | 1.  |              | •   |
|     |             |             | 1075                    | 5           |             | <i>'</i> .  |             | 1086        | )          |             | : :        |             | 108        | 5          |             | Lys         |     | /*·          | ٠.  |
|     |             | 1090        | )                       |             | •           |             | 1099        | 5           |            |             |            | 1100        | 0          |            |             | Thr         | Ž.  |              |     |
|     | 1105        | 5.          | •                       |             |             | 1110        | ) ,         | •           |            |             | 111!       | 5           | <b>*</b> ! |            |             | Cys : 1120  |     |              |     |
|     |             |             |                         | • •         | 112         | 5           |             |             | Ca.        | 1130        | )          |             |            | ٠.,        | 1139        |             |     | 5 11<br>1423 | .1. |
|     |             |             |                         | 1140        | )           |             | _           |             | 114        | 5           |            |             |            | 115        | 0           | His 🗀       |     | :- 3**       |     |
|     | _           |             | 1155                    | 5           | -           |             |             | 116         | 0          |             |            | '           | 116        | 5          |             | Trp         |     |              |     |
|     |             | 1170        | )                       |             |             |             | 117         | 5           |            |             |            | 1180        | )          |            |             | Arg         | * . |              |     |
|     | 1185        | 5           | _                       |             |             | 1190        | ) .         | •           | -          |             | 119        | 5           | ÷ ,*       |            | Lys         | 1200        |     |              |     |
|     | Pro         | Arg         | Lys                     | Asp         | Leu<br>120  |             | Val         |             | Leu        |             |            | Thr         | Asp        | Val        | Asn<br>121  | Lys .       |     |              |     |

| ГÀà                                                   | Asp                                     | Lys                                                                         | Gln<br>1220                                                   | _                                                                              | Arg                                                           | Thr                                            | Ala                                           | Leu<br>1225                             |                                                                      | Leu                                                         | Ala                                               | Ser                                                                 | Ala<br>1230                                   |                                                               | Gly                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |         |
|-------------------------------------------------------|-----------------------------------------|-----------------------------------------------------------------------------|---------------------------------------------------------------|--------------------------------------------------------------------------------|---------------------------------------------------------------|------------------------------------------------|-----------------------------------------------|-----------------------------------------|----------------------------------------------------------------------|-------------------------------------------------------------|---------------------------------------------------|---------------------------------------------------------------------|-----------------------------------------------|---------------------------------------------------------------|---------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| Asn                                                   | Ser                                     | Glu<br>123                                                                  |                                                               | Val                                                                            | Lys                                                           |                                                | Leu<br>1240                                   |                                         | Asp                                                                  | Arg                                                         |                                                   | Cys<br>1245                                                         |                                               | Leu                                                           | Asn                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |         |
| Val                                                   | Leu<br>1250                             | -                                                                           | .Asn                                                          | Lys                                                                            | Lys                                                           | Arg<br>1255                                    |                                               | Ala                                     | Leu                                                                  | Ile                                                         | Lys<br>1260                                       |                                                                     | Val                                           | Gln                                                           | Cys                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |         |
| 126                                                   | 5                                       | _                                                                           |                                                               | 7                                                                              | 1270                                                          | )                                              |                                               | •                                       |                                                                      | 1275                                                        | 5                                                 |                                                                     |                                               | . 1 . "                                                       | Pro<br>1280                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | ٠.      |
| ,Asn                                                  | Ile                                     | Pro                                                                         | Asp                                                           | Glu<br>128                                                                     | Tyr<br>5                                                      | Gly                                            | Asn                                           | Thr                                     | Thr<br>1290                                                          |                                                             | His                                               | Tyr                                                                 | Ala                                           | Ile<br>1295                                                   |                                                               | £                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |         |
|                                                       |                                         | _                                                                           | 1300                                                          | )                                                                              | Met                                                           | 11 17                                          |                                               | 1309                                    | 5                                                                    |                                                             |                                                   |                                                                     | 1310                                          | )                                                             | - ;;                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | ٠.      |
|                                                       |                                         | 131                                                                         | 5                                                             |                                                                                | Lys                                                           | ij                                             | 1320                                          | 3                                       |                                                                      |                                                             | ,                                                 | 1325                                                                | 5                                             |                                                               |                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |         |
|                                                       | 1330                                    | )                                                                           | 13                                                            |                                                                                | Gln                                                           | 1335                                           | ,                                             | F                                       |                                                                      |                                                             | 1340                                              | ) ်                                                                 |                                               |                                                               |                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |         |
| 1345                                                  | 5                                       |                                                                             |                                                               | ٠, ٠                                                                           | 1350                                                          | )                                              |                                               | *.                                      |                                                                      | 1355                                                        | õ                                                 |                                                                     |                                               | · · '                                                         | Ala<br>1360                                                   | ن ڏڻي ا                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |         |
|                                                       |                                         |                                                                             |                                                               | 136                                                                            | 5 ⊬છે                                                         |                                                |                                               |                                         | 1370                                                                 | ) · "                                                       |                                                   |                                                                     |                                               | 1379                                                          |                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | į į , . |
| :                                                     |                                         |                                                                             | 1380                                                          | )                                                                              | Gln                                                           |                                                |                                               | 1385                                    | 5 ,                                                                  |                                                             |                                                   |                                                                     | 1390                                          | )                                                             |                                                               | , ,                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | -       |
|                                                       |                                         | 139                                                                         | 5                                                             |                                                                                | His                                                           | •                                              | 1400                                          | )                                       |                                                                      |                                                             |                                                   | 1405                                                                | õ                                             |                                                               |                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | `       |
| _                                                     | 1410                                    | ) = ;                                                                       | 1 1                                                           |                                                                                | Leu                                                           | 1415                                           | 5                                             | ·                                       |                                                                      |                                                             | 1420                                              | ) '                                                                 | ,                                             |                                                               |                                                               | 111                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | •       |
| Gln<br>1425                                           |                                         | Leu                                                                         |                                                               | Leu                                                                            | Thr 1430                                                      |                                                | Glu:                                          | Glu                                     | Glu                                                                  | Ser<br>1435                                                 |                                                   | Arg                                                                 | Phe                                           | Lys                                                           | Gly 1440                                                      | · .*                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |         |
|                                                       |                                         | Asn                                                                         |                                                               |                                                                                | Pro                                                           |                                                | Lýs                                           | Met                                     | Ser                                                                  |                                                             |                                                   | Pxo                                                                 | Gĺu                                           | Ile                                                           |                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |         |
|                                                       |                                         |                                                                             |                                                               | 1445                                                                           | 5 😌                                                           |                                                | _                                             |                                         | 1450                                                                 | )                                                           |                                                   |                                                                     |                                               | 1455                                                          | 5                                                             | i                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |         |
| _                                                     |                                         |                                                                             | 1460                                                          | )                                                                              | Glu                                                           | 1:1                                            |                                               | 1465                                    | 5                                                                    |                                                             | 1 1                                               |                                                                     | 1470                                          | )                                                             | 4.65                                                          | r                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |         |
|                                                       |                                         | 1475                                                                        | 5                                                             |                                                                                |                                                               | 7                                              | 1480                                          | )                                       |                                                                      | ٠                                                           |                                                   | 1485                                                                | 5                                             |                                                               | Gly                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |         |
|                                                       | 1490                                    | )                                                                           | Asn                                                           | GTÄ                                                                            | Lèu                                                           | 11e <sup>2</sup>                               |                                               | GTU                                     | Arg                                                                  | ràs.                                                        | Ser                                               | Arg                                                                 | rnr                                           | PTO                                                           | GIU                                                           | •                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |         |
| Asn<br>1505                                           |                                         | ~ ~                                                                         |                                                               |                                                                                | _                                                             |                                                |                                               |                                         | <b>~</b> 7                                                           | .071                                                        | 1500                                              | ) 🏋                                                                 |                                               |                                                               |                                                               | 1 .                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |         |
|                                                       |                                         | Gln                                                                         |                                                               | Pro                                                                            | Asp<br>1510                                                   | Asn                                            |                                               | Ser                                     | Glu                                                                  |                                                             | Tyr                                               | ) 🏋                                                                 |                                               |                                                               | Cys                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |         |
|                                                       | 5                                       |                                                                             | 1.                                                            | 11.                                                                            | 1510<br>Tyr                                                   | 'Asn'<br>)                                     | Glu                                           |                                         |                                                                      | 1515<br>Met                                                 | Tyr                                               | His                                                                 | Arg                                           | Ile                                                           | Cys<br>1520<br>Ser                                            | )                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |         |
| Glu                                                   | Leu                                     | Val                                                                         | Ser                                                           | Asp<br>1525<br>Pro                                                             | 1510<br>Tyr<br>Glu                                            | Asn<br>)<br>Lys                                | Glu<br>Glu                                    | Lys                                     | Gln<br>1530<br>Lys                                                   | 1515<br>Met<br>)^                                           | Tyr<br>Pro                                        | His<br>Lys                                                          | Arg<br>Tyr                                    | Ile<br>Ser<br>1535<br>Glu                                     | Cys<br>1520<br>Ser                                            | 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |         |
| Glu<br>Glu                                            | Leu<br>Asn                              | Val<br>Ser                                                                  | Ser<br>Asn<br>1540<br>Leu                                     | Asp<br>1525<br>Pro                                                             | 1510<br>Tyr<br>Glu                                            | Asn<br>Lys<br>Gln<br>Ser                       | Glu<br>Glu<br>Asp                             | Lys<br>Leu<br>1545<br>Asn               | Gln<br>1530<br>Lys                                                   | 1515<br>Met<br>)<br>Leu                                     | Tyr<br>Pro<br>Thr                                 | His<br>Lys<br>Ser                                                   | Arg<br>Tyr<br>Glu<br>1550<br>Lys              | Ile<br>Ser<br>1535<br>Glu                                     | Cys<br>1520<br>Ser<br>Glu                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |         |
| Glu<br>Glu<br>Ser<br>Gln                              | Leu<br>Asn<br>Gln<br>Glu<br>1570        | Val<br>Ser<br>Arg<br>1555<br>Pro                                            | Ser<br>Asn<br>1540<br>Leu<br>Glu                              | Asp<br>1525<br>Pro<br>)<br>Glu                                                 | Tyr<br>Glu<br>Gly<br>Asn                                      | Asn<br>Lys<br>Gln<br>Ser<br>Lys<br>1575        | Glu<br>Asp<br>Glu<br>1560<br>Asp              | Lys<br>Leu<br>1545<br>Asn<br>)          | Gln<br>1530<br>Lys<br>Gly<br>Asp                                     | 1515<br>Met<br>)^<br>Leu<br>Gln<br>Arg                      | Tyr Fro Thr Pro Glu 1580                          | His<br>Lys<br>Ser<br>Glu<br>1565<br>Leu                             | Arg Tyr Glu 1550 Lys Glu Glu                  | Ile<br>Ser<br>1535<br>Glu<br>)<br>Arg<br>Asn                  | Cys<br>1520<br>Ser<br>Glu<br>Ser                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |         |
| Glu<br>Glu<br>Ser<br>Gln<br>Met<br>1585               | Leu<br>Asn<br>Gln<br>Glu<br>1570<br>Ala | Val<br>Ser<br>Arg<br>1555<br>Pro                                            | Ser<br>Asn<br>1540<br>Leu<br>Glu<br>Glu                       | Asp<br>1525<br>Pro<br>)<br>Glu<br>Ile<br>Glu                                   | 1510<br>Tyr<br>Glu<br>Gly<br>Asn<br>Met<br>1590               | Asn<br>Lys<br>Gln<br>Ser<br>Lys<br>1575<br>Lys | Glu<br>Asp<br>Glu<br>1560<br>Asp              | Lys<br>Leu<br>1545<br>Asn<br>Gly<br>His | Gln<br>1530<br>Lys<br>Gly<br>Asp                                     | 1515<br>Met<br>)<br>Leu<br>Gln<br>Arg<br>Ser<br>1595        | Tyr Fro Thr Pro Glu 1580 Thr                      | His<br>Lys<br>Ser<br>Glu<br>1565<br>Leu                             | Arg Tyr Glu 1550 Lys Glu Val                  | Ser<br>1535<br>Glu<br>Arg<br>Asn                              | Cys<br>1520<br>Ser<br>Glu<br>Ser<br>Phe<br>Phe<br>1600        | . ;                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |         |
| Glu<br>Glu<br>Ser<br>Gln<br>Met<br>1585<br>Pro        | Leu Asn Gln Glu 1570 Ala                | Val<br>Ser<br>Arg<br>1555<br>Pro<br>Ile<br>Asn                              | Asn<br>154(<br>Leu<br>Glu<br>Glu<br>Leu                       | Asp<br>1525<br>Pro<br>)<br>Glu<br>Ile<br>Glu<br>Thr                            | 1510<br>Tyr<br>Glu<br>Gly<br>Asn<br>Met<br>1590<br>Asn        | Asn Lys Gln Ser Lys 1575 Lys                   | Glu Asp Glu 1560 Asp Lys                      | Lys Leu 1545 Asn Gly His                | Gln<br>1530<br>Lys<br>Gly<br>Asp<br>Gly<br>Ala<br>1610               | 1515<br>Met<br>)<br>Leu<br>Gln<br>Arg<br>Ser<br>1595<br>Gly | Tyr Pro Thr Pro Glu 1580 Thr                      | His<br>Lys<br>Ser<br>Glu<br>1565<br>Leu<br>His                      | Arg Tyr Glu 1550 Lys Glu Val Asp              | Ser<br>1535<br>Glu<br>)<br>Arg<br>Asn<br>Gly<br>Asp<br>1615   | Cys<br>1520<br>Ser<br>Glu<br>Ser<br>Phe<br>Phe<br>1600<br>Gly | •                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |         |
| Glu<br>Glu<br>Ser<br>Gln<br>Met<br>1585<br>Pro<br>Leu | Leu Asn Gln Glu 1570 Ala Glu Ile        | Val<br>Ser<br>Arg<br>1555<br>Pro<br>Ile<br>Asn                              | Asn<br>1540<br>Leu<br>Glu<br>Glu<br>Leu<br>Pro<br>1620        | Asp<br>1525<br>Pro<br>)<br>Glu<br>Ile<br>Glu<br>Thr<br>1605<br>Arg             | 1510<br>Tyr<br>Glu<br>Gly<br>Asn<br>Met<br>1590<br>Asn        | Asn Lys Gln Lys 1575 Lys Gly Ser               | Glu Asp Glu 1560 Asp Lys Alla                 | Lys Leu 1545 Asn Gly His Thr            | Gln<br>1530<br>Lys<br>Gly<br>Asp<br>Gly<br>Ala<br>1610<br>Pro        | 1515 Met  Leu  Gln  Arg  Ser 1595 Gly  Glu                  | Tyr Pro Thr Pro Glu 1580 Thr Asn                  | His<br>Lys<br>Ser<br>Glu<br>1565<br>Leu<br>His<br>Gly               | Arg Tyr Glu 1550 Lys Glu Val Asp Gln 1630     | Ser<br>1535<br>Glu<br>Arg<br>Asn<br>Gly<br>Asp<br>1615<br>Phe | Cys<br>1520<br>Ser<br>Glu<br>Ser<br>Phe<br>Phe<br>1600<br>Gly |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |         |
| Glu Glu Ser Gln Met 1585 Pro Leu Asp                  | Leu Asn Gln 1570 Ala Glu Ile            | Val<br>Ser<br>Arg<br>1555<br>Pro<br>Ile<br>Asn<br>Pro<br>Glu<br>1635        | Asn<br>1540<br>Leu<br>Glu<br>Glu<br>Leu<br>Pro<br>1620<br>Asn | Asp<br>1525<br>Pro<br>Glu<br>Lle<br>Glu<br>Thr<br>1605<br>Arg                  | 1510<br>Tyr<br>Glu<br>Gly<br>Asn<br>Met<br>1590<br>Asn<br>Lys | Asn Lys Gln Lys 1575 Lys Gly Ser               | Glu Glu Asp Glu 1560 Asp Lys Alla Arg         | Lys Leu 1545 Asn Gly His Thr 1625 Ser   | Gln<br>1530<br>Lys<br>Gly<br>Asp<br>Gly<br>Ala<br>1610<br>Pro        | 1515 Met  Leu  Gln  Arg  Ser 1595 Gly  Glu  Glu             | Pro Thr Pro Glu 1580 Thr Asn Ser                  | His<br>Lys<br>Ser<br>Glu<br>1565<br>Leu<br>His<br>Gly<br>Gln<br>Asn | Arg Tyr Glu 1550 Lys Glu Val Asp Gln 1630 Asp | Ser<br>1535<br>Glu<br>Arg<br>Asn<br>Gly<br>Asp<br>1615<br>Phe | Cys<br>1520<br>Ser<br>Glu<br>Ser<br>Phe<br>1600<br>Gly<br>Pro | and the second of the second o |         |
| Glu Glu Ser Gln Met 1585 Pro Leu Asp                  | Leu Asn Gln Glu 1570 Ala Glu Ile Thr    | Val<br>Ser<br>Arg<br>1555<br>Pro<br>Ile<br>Asn<br>Pro<br>Glu<br>1635<br>Phe | Asn<br>1540<br>Leu<br>Glu<br>Glu<br>Leu<br>Pro<br>1620<br>Asn | Asp<br>1525<br>Pro<br>)<br>Glu<br>Ile<br>Glu<br>Thr<br>1605<br>Arg<br>)<br>Glu | Glu Gly Asn Met 1590 Asn Lys Glu Glu                          | Asn Lys Gln Lys 1575 Lys Gly Ser Tyr Gln 1655  | Glu Asp Glu 1560 Asp Lys Ala Arg His 1640 Asn | Lys Leu 1545 Asn Gly His Thr 1625 Ser   | Gln<br>1530<br>Lys<br>Gly<br>Asp<br>Gly<br>Ala<br>1610<br>Pro<br>Asp | 1515 Met  Leu  Gln Arg  Ser 1595 Gly  Glu  Glu  Ile         | Tyr Pro Thr Pro Glu 1580 Thr Asn Ser Gln Leu 1660 | His Lys Ser Glu 1565 Leu His Gly Gln Asn 1645                       | Arg Tyr Glu 1550 Lys Glu Val Asp Gln 1630 Asp | Ser<br>1535<br>Glu<br>Arg<br>Asn<br>Gly<br>Asp<br>1615<br>Phe | Cys<br>1520<br>Ser<br>Glu<br>Ser<br>Phe<br>1600<br>Gly<br>Pro | and the second                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |         |

Glu Leu Ser Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn
1685

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1705

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360 3.65 355 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu 370 '- '375 380 Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys 395 390 Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu 405 410 Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn 425 420 Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro 440 Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu 455 460 Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu 470 475 Lys Gin Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gin Asp 485 490 Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu 500 505 Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys 520 525 Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly 535 540 Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser 550 555 Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr 565 570 His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln 585 Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln 600 Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys 615 620 Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile 630 635 Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu 645 650

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105, 105, 105, 100 and 100 and

DEICHOCHE JAM - 015163263 1 -

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| Leu        | Asp        | Arg<br>195 | Arg        | Суз        | Gln        | Leu        | Asn<br>200 | Val        | Leu        | Asp        | Asn         | Lys<br>205 | Lys        | Arg        | Thr        |
| Ala        | Leu<br>210 | Ile        | Lys        | Ala        | Val        | Gln<br>215 | Cys        | Gln        | Glu        | Asp        | Glu<br>220  | Cys        | Ala        | Leu        | Met        |
| 225        |            |            |            |            | Thr<br>230 |            | •          |            |            | 235        |             |            |            |            | 240        |
| Thr        |            |            |            | 245        | Ala        |            |            |            | 250        |            |             |            |            | 255        |            |
|            |            |            | 260        |            | Gly        |            |            | 265        |            |            |             |            | 270        |            |            |
|            |            | 275        |            | • ;        | Leu        |            | 280        |            |            |            | ·           | 285        | ,          |            |            |
| _          | 290        |            |            |            | Lys        | 295        |            |            |            |            | 300         |            |            |            |            |
| 305        | _          |            |            |            | Ile<br>310 |            |            | •          |            | 315        |             |            |            |            | 320        |
|            |            |            |            | 325        | Glu        |            |            |            | 330        |            |             |            |            | 335        |            |
|            | _          |            | 340        |            | Arg        | •          |            | 345        |            |            |             |            | 350        |            |            |
|            |            | 355        |            |            | Ser        | •          | 360        |            |            |            | •           | 365        |            |            |            |
|            | 370        |            | .*         | ,          | Asn        | 375        |            | •          |            |            | 380         | -          |            |            |            |
| 385        |            |            | 4          |            | Phe<br>390 |            |            |            |            | 395        |             |            |            | •          | 400        |
|            |            |            |            | 405        | Glu        |            |            |            | 410        |            |             |            |            | 415        |            |
|            |            |            | 420        |            | His        |            |            | 425        |            |            |             |            | 430        |            |            |
|            |            | 435        | •          |            | •          |            | 440        | •          |            |            |             | 445        |            |            | Pro        |
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| 465        |            |            |            |            | 470        |            | ٠.         |            |            | 475        |             | eria de    |            |            | Glu<br>480 |
|            |            |            |            | 485        |            |            |            | ٠,         | 490        |            |             | 12 11      |            | 495        | Asp        |
|            | _          |            | 500        |            | •          |            |            | 505        |            | ,          |             | • .        | 510        |            | Glu        |
|            | _          | 515        |            |            |            |            | 520        |            |            | · •        | , -,,       | 525        |            |            | Asp        |
| _          | 530        |            |            | Leu        | Glu        | Asn<br>535 | Phe        | Met        | Ala        | Ile        | G1 u<br>540 | GLu        | Met        |            | Lys        |
| 545        |            | •          |            |            | 550        | •          |            | ٠          | 20         | 555        |             |            |            |            | Ala<br>560 |
| Thr        | Ala        | Gly        | Asn        | Gly<br>565 |            | Asp        | Gly        | Leu        | 11e<br>570 | Pro        | Pro         | Arg        | . Lys      | Ser<br>575 | Arg        |
|            |            |            |            |            |            |            |            |            |            |            |             |            |            |            |            |

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 ggcccaaggc cccaagtata tcaaggcact tgggcagaac atgccaagga atcaaatgtc 2520
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 aagccccct ggggatttgg tttggtcttg tgatcaggtg gtctatgggg ctatccctac 2700
 aaagaagaat ccagaaatag gggcacattg aggaatgata ctgagcccaa agagcattca 2760
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 gttatgaaga tggttgaaca ccccacacat agcaccggag atatgagatc aacagtttct 2880
 tagecataga gatteacage ecagageagg aggaegetge acaccatgea ggatgaeatg 2940
 ggggatgcgc tcgggattgg tgtgaagaag caaggactgt tagaggcagg ctttatagta 3000
 acaagacggt ggggcaaact ctgatttccg tgggggaatg tcatggtctt gctttactaa 3060
 gttttgagac tggcaggtag tgaaactcat taggctgaga accttgtgga atgcagctga 3120
 cccagctgat agaggaagta gccaggtggg agcctttccc agtgggtgtg ggacatatct 3180
 ggcaagattt tgtggcactc ctggttacag atactggggc agcaaataaa actgaatctt 3240
                                                                                                                                                                                                                                                                                           3279
 gttttcagac cttaaaaaaa aaaaaaaaa aaaagtttt
 <210> 383
 <211> 154
 <212> PRT
                                                                                                                  Control to the Control of the Contro
 <213> Homo sapiens and the same and the same
                                                                                    ing the fill of the thirty of the first term of the second of the second
 <400> 383
Met Ala Gly Val Arg Asp Gln Gly Gln Gly Ala Arg Trp Pro His Thr
                                                                    5 10 15
Gly Lys Arg Gly Pro Leu Gln Gly Leu Thr Trp Ala Thr Gly Gly
His Cys Phe Ser Ser Glu Glu Ser Gly Ala Val Asp Gly Ala Gly Gln
Lys Lys Asp Arg Ala Trp Leu Arg Cys Pro Glu Ala Val Ala Gly Phe
                     \overline{\mathbf{50}} . The first \overline{\mathbf{50}} is \overline{\mathbf{50}} in \overline{\mathbf{50} in \overline{\mathbf{50}} in \overline{\mathbf{50}} in \overline{\mathbf{50} in \overline{\mathbf{50}} in \overline{\mathbf{50} in \overline{\mathbf{50}}
 Pro Leu Gly Ser Asp Cys Arg Glu Gly Gly Arg Gln Gly Cys Gly Gly
65 70 75 80
 Ser Asp Asp Glu Asp Asp Leu Gly Val Ala Pro Gly Leu Ala Pro Ala
Trp Ala Leu Thr Gln Pro Pro Ser Gln Ser Pro Gly Pro Gln Ser Leu
                                                                                                                                         105
 Pro Ser Thr Pro Ser Ser Ile Trp Pro Gln Trp Val Ile Leu Ile Thr
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       130
Ala Leu Glu Arg Gly His Leu Val Arg Glu
145

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<211> 557

<212> DNA

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ggggaagggt cccttttgca ttgccaagtg ccataaccat gagcactact ctaccatggt 180 🗀 🗀
tctgcctcct ggccaagcag gctggtttgc aagaatgaaa tgaatgattc tacagctagg 240
acttaacett gaaatggaaa gtettgeaat eecatttgea ggateegtet gtgeacatge 300 4004
ctctgtagag agcagcattc.ccagggacct tggaaacagt tggcactgta aggtgcttgc 360
tococaagac acatoctaaa aggtgttgta atggtgaaaa ogtottoott otttattgcc 420 %
ccttcttatt tatqtqaaca actqtttqtc tttttttgta tcttttttaa actgtaaagt 480
tcaattgtga aaatgaatat catgcaaata aattatgcga ttttttttc aaagtaaaaa 540

        aaaaaaaaaa
        aaaaaaaaa
        from the control of the control o
<213> Homo sapiens
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teteaaagee atetgetgte ttegagtaeg gacacateat cacteetgea ttgttgatea 180
aaacgtggag gtgcttttcc tcagctaaga agcccttagc aaaagctcga atagacttag 240
tatcagacag gtccagtttc cgcaccaaca cctgctggtt ccctgtcgtg gtctggatct/300
ctttggccac caattccccc ttttccacat cccggca
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<211> 300
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gcccgctcgg cccagagggt gggcgcgggg ctgcctctac cggctggcgg ctgtaactca 120
gcgaccttgg cccgaaggct ctagcaagga cccaccgacc ccagccgcgg cggcggcggc 180
geggaetttg eeeggtgtgt ggggeggage ggaetgegtg teegeggaeg ggeagegaag 240
atgttagect tegetgecag gacegtggac egateceagg getgtggtgt aaceteagee 300
<210> 387
                       医乳球 美国 化邻氯 化硫酸铁 斯拉尔特 医抗气性病 医抗肾炎 医肺炎 化二氯甲基乙基
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<212> DNA
<400> 387
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ecceptecty typecateaty ateageacet atgagttegy casaagette tteeagagge 120
```

```
tqaaccagga ccgqcttctg ggcgqctqaa agggcaagg aggcaaggac cccgtctctc 180
ccacqqatqq qqaqaqqqca qqaqqaqacc caqccaaqtq ccttttcctc aqcactqaqq 240
gagggggett gtttcccttc cctcccqqcq acaaqctcca gggcagggct gtccctctqq 300
qcqqcccaqc acttcctcaq acacaacttc ttcctqctqc tccaqtcqtq gqqatcatca 360
cttacccacc ccccaagtte aagaccaaat cttccagctg cccccttcgt gtttccctgt 420
gtttgctgta gctgggcatg tctccaggaa ccaagaagcc ctcagcctgg tgtagtctcc 480
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<211> 520
<212> DNA
<213> Homo sapiens
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gtttgaagat tgcctcttct acagcttctg agaattgtgt tatttcactt gccaagtgaa 180
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ccaggaaact gctacttgtg gacctcacca gagaccagga gggtttggtt agctcacagg 300
acttccccca ccccagaaga ttagcatccc atactagact catactcaac tcaactaggc 360
tcatactcaa ttgatggtta ttagacaatt ccatttettt etggttatta taaacagaaa 420
atctttcctc ttctcattac cagtaaaggc tcttggtatc tttctgttgg aatgatttct 480
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<211> 365
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<213> Homo sapiens
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aacgactttc caaataatct caccagegee ttecagetca ggegteetag aagegtettg 180
aagectatgg ccagetgtet ttgtgtteee teteaceege etgteeteac agetgagaet 240
eccaggaaac etteagaeta cetteetetg eetteageaa ggggegttge ecacattete 300
tgagggtcag tggaagaacc tagactccca ttgctagagg tagaaagggg aagggtgctg 360
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<210> 390
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tacacggntt ctcatgggtg tggaacatct ctgcttgcgg tttcaggaag gcctctggct 120
gctctangag tctgancnga ntcgttgccc cantntgaca naaggaaagg cggagcttat 180
tcaaagtcta gagggagtgg aggagttaag gctggatttc a
<210> 391
<211> 325
<212> DNA
<213> Homo sapiens
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tagccagggc actgctgcca acagccagtc cnnataccat catgtnaccc ggtgngctct 180
naantingat niccanagec ciacceaten tagticiget cicceacegg niaccagece 240
cactgoccag gaatectaca gecagtacce tgtcccgacg tetetaceta ccagtacgat 300
gagaceteeg getaetaeta tgace
            ි උන් 1150 කි. මුදු වන්නේ දෙන්නේ ප්රවේඛ දෙන්න් කියල් වන වන
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agteteaett nggenagngn etectaettg agtetettee eeggeetgnn eeagtngnaa 120
antaccanga accgncatgn ettaanaacn neetggtttn tgggttnnte aatgactgea 180
tgcagtgcac caccctgtcc actacgtgat gctgtaggat taaagtctca cagtgggcgg 240
ctgaggatac agcgccgcgt cctgtgttgc tggggaa
<210> 366

<211> 566

<212> DNA
<213> Homo sapiens

</
                                                           (-4) = \epsilon_{\lambda_1} + \frac{1}{\epsilon_{\lambda_1}} \epsilon_{\lambda_2} + \frac{1}{\epsilon_{\lambda_1}} \epsilon_{\lambda_2} + \frac{\lambda_{\lambda_2}}{\epsilon_{\lambda_1}} \epsilon_{\lambda_2}
<400> 393
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ttgccgggaa cactgcagag acaatgctgt gagtttccaa ccttagccca tctgcgggcal 180
gagaaggtct agtttgtcca tcagcattat catgatatca ggactggtta cttggttaag 240
gaggggteta ggagatetgt ccettttaga gacacettae ttataatgaa gtatttggga 300
gggtggtttt caaaagtaga aatgtcctgt attccgatga tcatcctgta aacattttat 360
catttattaa tcatccctqc ctqtqtctat tattatattc atatctctac qctqqaaact 420
ttctgcctca atgtttactg tgcctttgtt tttgctagtt tgtgttgttg aaaaaaaaa 480
cattetetge etgagtttta atttttqtee aaaqttattt taatetatae aattaaaage 540
ttttgcctat caaaaaaaa aaaaaa
                                                                       566
<210> 394
The set of Engineer by the Arisky and Committee of the Committee of
<220>
<221> misc_feature
                                                                         5 8 3.833
<222> (1)...(384)
                                                                           1 3.
<223> n = A, T, C or G
```

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  gcaggaggac cgggctttaa ggagttttaa gctgagtgtc actgtagacc ccaaatacca 180
  teccaagatt ategggagaa agggggeagt aattacecaa ateeggttgg ageatgaegt 240
  gaacatccag tttcctgata aggacgatgg gaaccagccc caggaccaaa ttaccatcac 300
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  <210> 395
  <211> 399
  <212> DNA
  <213> Homo sapiens
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  tetgacettg gaetecaaga ectacateaa eageetgget atattagatg atgagecagt 120
  tatcagaggt ttcatcattg cggaaattgt ggagtctaag gaaatcatgg cctctgaagt 180
  atteacgtet ttecagtace etgagttete tatagagttg cetaacacag geagaattgg 240 ceagetactt gtetgeaatt gtatetteaa gaataceetg geeateeett tgaetgaegt 300
   caagttetet ttggaaagee tgggeatete eteactacag acetetgace atgggaeggt 360
   gcagcctggt gagaccatcc aatcccaaat aaaatgcac
                                                                      399.
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   <211> 403
   <212> DNA
   <213> Homo sapiens
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   gacattttca acttctgctc cagctgctga taaaacaaat catgtgttta gcttgactcc 120
   agacaaggac aacctgttcc ttcataactc tctagagaaa aaaaggagtt gttagtagat 180
   actaaaaaaa gtggatgaat aatctggata tttttcctaa aaagattcct tgaaacacat 240
   taggaaaatg gagggcctta tgatcagaat gctagaatta gtccattgtg ctgaagcagg 300
   gtttagggga gggagtgagg gataaaagaa ggaaaaaaag aagagtgaga aaacctattt 360
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   <210> 397
   <211> 100
   <212> DNA
   <213> Homo sapiens
   <220>
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   <222> (1)...(100)
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   tocatococg ctcctggttg gtnacagaat gactgacaaa
   <210> 398
   <211> 278
```

```
<212> DNA
         <213> Homo sapiens
                                                                                                                                                                                     in the supplier of the state of the supplier of the state of the supplier of the state of the supplier of the 
         <220>
                                                                                                                                                                              on after the problem of the country of closers in the country of t
         <221> misc feature
   <222> (1) ... (278)
                                                                                                                                                                                                                   ာ အောက်များကို သည်သည့်သည်။ ထိုက်မှာမြောက်သည် နောက်
         <223> n = A, T, C or G
                                                                                                                                                                                         Color of the state of the second
        <400> 398
        geggeeget egacageagt teegeeageg etegeeeetg ggtggggatg tgetgeaege 60
        ccacctggac atctggaagt cagcggcctg gatgaaagag cggacttcac ctggggcgat 120
        teactactgt geetegacea gtgaggagag etggacegae agegaggtgg acteateatg 180
        ctccgggcag cccatccacc tgtggcagtt cctcaaggag ttgctactca agccccacag 240
        ctatggccgc ttcattangt ggctcaacaa ggagaagg
        <210> 399
 298 1000 Burgaria (2000)
        <212> DNA COMPANIE OF THE PROPERTY OF CHARLES OF THE PROPERTY 
       <213> Homo sapiens
(2) A separate of the same of the sam
                                                                                                                                                                                                                       COMPARTING THE STATE OF THE STATE SHELL I
        <222> (1)...(298)
        <223> n = A, T, C or G
        <400> 399
        acggaggtgg aggaagcgnc cctgggatcg anaggatggg tcctgncatt gaccncctcn 60
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        ecgagatega gegeatggge etggteatgg acegeatggg etecgtggag egeatggget 180
        coggeattga gogeatggge cogetgggee togaccaeat ggeeteeane attganogea 240
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       <210> 400
        <211> 548
        <212> DNA
        <213> Homo sapiens
                                                                                                                                                    grands are exercised as the contract of the co
                                                                                                                                                                                                                                                                                               [400> 400] 18/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 19/10 1
  , acateaacta ettécteatt ttaaggtäté geägtteect teateceett étectgeett 60% (
gtacatgtac atgtatgaaa tttccttctc ttaccgaact ctctccacac atcacaaggt 120
  caaagaacca cacgettaga agggtaagag ggcaccetat gaaatgaaat ggtgatttet 180
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       tgcagagggc tagagaatta tttcatacag gctttgaggc cacccatgtc acttatcccg 300
       tatacectet caccatecce ttgtctacte tgatgecece aagatgeaac tgggeageta 360
       gttggcccca taattctggg cetttgttgt ttgttttaat tacttgggca teccaggaag 420
       ctttccagtg atctcctacc atgggccccc ctcctgggat caagccctc ccaggccctg 480
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      agcaggtt
       <210> 401
       <211> 355
       <212> DNA
       <213> Homo sapiens
                                                                                                                                                        i i mortuuri on 10 kii ja mortuuri on 1900.
Heriotaan on 1909
      <220>
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      <222> (1)...(355)
      <223> n = A, T, C or G
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<400> 401
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taagagtggt ggcctatttc agctgctttg acaaaatgac tggctcctga cttaacgttc 180
tataaatgaa tgtgctgaag caaagtgccc atggtggcgg cgaagaagan aaagatgtgt 240
tttgttttgg actctctgtg gtcccttcca atgctgnggg tttccaacca ggggaagggt 300
cccttttgca ttgccaagtg ccataaccat gagcactact ctaccatggn tctgc
<210> 402
<211> 407
<212> DNA
<213> Homo sapiens
<220> ↔
<221> misc_feature '
<222> (1)...(407)
<223> n = A, T, C or G
<400> 402
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aaatggaaaa cagaaaaaag caggtgttgc actcctactt tctgacaaaa cagactatgc 180
gaataaagat aaaaaagaga aggacattac aaaggtggtc ctgacctttg ataaatctca 240
ttgcttgata ccaacctggg ctgttttaat tgcccaaacc aaaaggataa tttgctgagg 300
ttgtggagct tctcccctgc agagagtccc tgatctccca aaatttggtt gagatgtaag 360
gntgattttg ctgacaactc cttttctgaa gttttactca tttccaa

    Section 1. The section of the section 
<210> 403
<211> 303
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(303)
<223> n = A, T, C or G
<400> 403
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tootaagoaa gagocatggo atggtgaaaa tgcaaaagga gagtotggoo aatotacaaa 120 🕟 🔄
tagagaacaa gacctactca gtcatgaaca aaaaggcaga caccaacatg gatctcatgg 180 ..........
gggattggat attgtaatta tagagcagga agatgacagt gatcgtcatt tggcacaaca 240
tottaacaac gaccgaaacc cattatttac ataaacctcc attcggtaac catgttgaaa 300
                                                                         in the figure time has a middle filler out to the first the 303 middle filler out to the filler out 
gga
<210> 404
                                                                                                                                                                                                          10.12
<211> 225
<212> DNA
<213> Homo sapiens
<400> 404
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attgttaatg cactcattta cctttacatg gtgaaagttc tctcttgatc ctacaaacag 120.
acattttcca ctcgtgtttc catagttgtt aagtgtatca gatgtgttgg gcatgtgaat 180
ctccaagtgc ctgtgtaata aataaagtat ctttatttca ttcat
<210> 405
```

```
<211> 334
  <212> DNA
  <213> Homo sapiens '
  <220>
                                                                                                 And the state of the state of
<221> misc_feature
                                                                                                and the water was a file
  <222> (1)...(334)
  <223> n = A, T, C or G
  gagctgttat actgtgagtt ctactaggaa atcatcaaat ctgagggttg tctggaggac 60
  ttcaatacac ctcccccat agtgaatcag cttccagggg gtccagtccc tctccttact 120
  teatececat eccatgeead aggaagacee teetecttg geteacagee ttetetagge 180'
  ttcccagtgc ctccaggaca gagtgggtta tgttttcagc tccatccttg ctgtgagtgt 240
  ctggtggggt tgtgcctcba gcttctgctc agtgcttcat ggacagtgtc cagcccatgt 300
  cactetecae teteteaning tggateceae, eeet
                                                                                                                                                                           334: 4
  <210> 406
  <211> 216
  <212> DNA
                                                                                        Services to the contract of the second property prime
  <213> Homo sapiens
                              which is the constant of the parameters of \Gamma and \Gamma , and \Gamma , and \Gamma
 <220> bei to possesse to en english for the condition of the page of the condition of the conference of the condition of
                                                                                                  The continuous games are also as a second second second
                                                                         <400> 406
 tttcatacct aatgagggag ttganatnac atnnaaccag gaaatgcatg gatctcaang 60%
 gaaacaaaca cccaataaac tcggagtggc agactgacaa ctgtgagaca tgcacttgct 120
 acnaaacaca aatttnatgt tgcacccttg tttctacacc tgtgggttat gacaaagaca 180
 actgccaaag aatnttcaag aaggaggact gccant
 <210> 407
 <211> 413
 <212> DNA
 <213> Homo sapiens
 <400> 407
 gctgacttgc tagtatcatc tgcattcatt gaagcacaag aacttcatgc cttgactcat 60
gtaaatgcaa taggattaaa aaataaattt gatatcacat ggaaacagac aaaaaatatt 120
 gtacaacatt gcacccagtg tcagattcta cacctggcca ctcaggaagc aagagttaat 180
 cccagaggte tatgtectaa tgtgttatgg caaatggatg teatgeaegt acetteattt 240
 ggaaaattgt catttgtcca tgtgacagtt gatacttatt cacatttcat atgggcaacc 300
 tgccagacag gagaaagtct tcccatgtta aaagacattt attatcttgt tttcctgtca 360
 tgggagttcc agaaaaagtt aaaacagaca atgggccagg ttctgtagta aag
 <210> 408
 <211> 183
 <212> DNA
 <213> Homo sapiens
                                          医结合结节的 医乳头结合 医海绵 网络罗马斯 医神经毒性 计重点自由的 计图片设计 医
 <221> misc_feature in the probability of the Approximation of the second of the second control of the second c
<223> n = A,T,C or G
                                                                           - Arbos of the stoom of Manground Burnelly Lyde Carryan Loyd
<400> 408
```

```
ggagctngcc ctcaattcct ccatntctat gttancatat ttaatgtctt ttgnnattaa 60
 tnettaacta gttaateett aaagggetan ntaateetta actagteeet eeattgtgag 120
 cattateett ecagtatten cettetnttt tatttactee tteetggeta eccatgtact 180
ntt
 <210> 409
 <211> 250
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <222> (1) ... (250)
 <223> n = A, T, C or G
 <400> 409
 cccacgcatg ataagctctt tatttctgta agtcctgcta ggaaatcatc aaatctgacg 60
 gtggtttggg ggacctgaac aaacctcctg taattaatca gctttcagtt tctccccta 120
 gtocctoctt caacaacata ggaggatoct coccttottt ctgctcacgg cottatctag 180
 gcttcccagt gcccccagga cagcgtgggc tatgtttaca gcgcntcctt gctggggggg 240
 ggccntatgc
 <210> 410
 <211> 306
 <212> DNA
 <213> Homo sapiens
 <220>
                                                    ing the second of the second o
 <221> misc_feature
 <222> (1)...(306)
 \langle 223 \rangle n = A,T,C or G
 qqctqqtttq caagaatgaa atgaatgatt ctacagctag gacttaacct tgaaatggaa 60
 agtottgcaa toccatttgc aggatocgto tgtgcacatg cototgtaga gagcagcatt 120
 cccagggacc ttggaaacag ttggcactgt aaggtgcttg ctccccaaga cacatcctaa 180
 aaggtgttgt aatggtgaaa accgcttcct tctttattgc cccttcttat ttatgtgaac 240
 nactggttgg ctttttttgn atcttttta aactggaaag ttcaattgng aaaatgaata 300
                                                                                                                                                     306
 tcntgc
 <210> 411
 <211> 261
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc feature
 <222> (1)...(261)
 <223> n = A, T, C or G
 <400> 411
 agagatattn cttaggtnaa agttcataga gttcccatga actatatgac tggccacaca 60
 ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
 tttaaatqtc tqaaatqqaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
 aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttacccat cagttccagc 240
 cttctctcaa ggngaggcaa a
```

```
<211> 241
   <212> DNA
<213> Homo sapiens
  <220>
  <221> misc_feature
  <222> (1)...(241)
  <223> n = A, T, C or G
  <400> 412
  gttcaatgtt acctgacatt tctacaacac cccactcacc gatgtattcg ttgcccagtg 60
  ggaacatacc agcctgaatt tggaaaaaat aattgtgttt cttgcccagg aaatactacg 120
  actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tggaggggag 180
  ctgggagatt tcactgggta cattgaattc ccaaactacc cangcaatta cccagccaac 240
  <210> 413
                                                       the second to the control policy at the control property of
  <211> 231
<212> DNA
                                                 in a contraction of the contraction of section (as in the
                                                                                               in the contraction of the programs and received
  <213> Homo sapiens
                                                                                                  The second of th
  <221> misc_feature
  <222> (1)...(231)
  <223> n = A, T, C or G
  <400> 413
 aactettaca atccaagtga etcatetgtg tgettgaate etttecactg tetcatetee 60
 ctcatccaag tttctagtac cttctctttg ttgtgaagga taatcaaact gaacaacaaa 120
 aagtttactc tcctcatttg gaacctaaaa actctcttct tcctgggtct gagggctcca 180
 agaatcettg aatcanttet cagatcattg gggacaccan atcaggaacc t
 <210> 414
 <211> 234
 <212> DNA
                                                                                                                              ingras t
 <213> Homo sapiens
 actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60
 gatggagctg aaaacataac ccactctgtc ctggaggcac tgggaagcct agagaaggct 120
gtgagccaag gagggagggt cttcctttgg catgggatgg ggatgaagta aggagaggga 180
ctggaccccc tggaagctga ttcactatgg ggggaggtgt attgaagtcc tcca
<210> 415
 <211> 217
 <212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(217)
<223> n = A, T, C or G
                                                                             المرافعة الم
                                                                                                                                                         4-1-6-5
                                                                            Thus there is speed to just
gcataggatt aagactgagt atcttttcta cattctttta actttctaag gggcacttct 60
caaaacacag accaggtage aaatctccac tgctctaagg ntctcaccac cactttctca 120
cacctagcaa tagtagaatt cagtcctact tctgaggcca gaagaatggt tcagaaaaat 180
antggattat aaaaaataac aattaagaaa aataatc
                                                                                                                                                                                                                                217
```

```
<210> 416
<211> 213
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature /
<222> (1)...(213)
<223> n = A, T, C or G
<400> 416
atgcatatnt aaagganact gcctcgcttt tagaagacat ctggnctgct ctctgcatga 60
ggcacagcag taaagctctt tgattcccag aatcaagaac tctccccttc agactattac 120
cgaatgcaag gtggttaatt gaaggccact aattgatgct caaatagaag gatattgact 180
atattggaac agatggagtc tctactacaa aag
<210> 417
<211> 303
<212> DNA
<213> Homo sapiens
                    \mathbf{p} = \mathbf{p} \cdot \mathbf{p}
<221> misc_feature
<222> (1) ... (303)
<223> n = A_r T_r C or G_r = \frac{1}{2} \frac{1}{
<400> 417
nagtetteag geceateagg gaagtteaca etggagagaa gteatacata tgtaetgtat 60
gtgggaaagg ctttactctg agttcaaatc ttcaagccca tcagagagtc cacactggag 120
agaagccata caaatgcaat gagtgtggga agagcttcag gagggattcc cattatcaag 180
ttcatctagt ggtccacaca ggagagaaac cctataaatg tgagatatgt gggaagggct 240
tcantcaaag ttcgtatctt caaatccatc ngaaggncca cagtatanan aaacctttta 300
agt
<210> 418
<211> 328
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(328)
<223> n = A, T, C or G
<400> 418
tttttggcgg tggtgggca gggacgggac angagtctca ctctgttgcc caggctggag 60
tgcacaggca tgatctcggc tcactacaac ccctgcctcc catgtccaag cgattcttgt 120
geeteageet teeetgtage tagaattaca ggeacatgee accaeacea getagttttt 180
gtatttttag tagagacagg gtttcaccat gttggccagg ctggtctcaa actcctnacc 240
teagnggtea ggetggtete aaacteetga ceteaagtga tetgeecace teagcetece 300
aaagtgctan gattacaggc cgtgagcc
<210> 419
<211> 389
<212> DNA
<213> Homo sapiens
<213> Homo sapiens
```

```
<220>
<221> misc feature
<222> (1)...(389)
<223> n = A,T,C or G' ...
<400> 419
cctcctcaag acggcctgtg gtccgcctcc cggcaaccaa gaagcctgca gtgccatatg 60
accectgage catggactgg agectgaaag geagegtaca ecetgeteet gatettgetg 120
cttgtttcct ctctgtggct ccattcatag cacagttgtt gcactgaggc ttgtgcaggc 180
cgagcaaggc caagctggct caaagagcaa ccagtcaact ctgccacggt gtgccaggca 240
cogettetec agecaccaac etcacteget ecegeaaatg geacateagt tettetacee 300
taaaggtagg accaaagggc atctgctttt ctgaagtcct ctgctctatc agccatcacg 360
<211> 408
<212> DNA
<213> Homo sapiens
<400> 420
gttcctccta actcctgcca gaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gteccattga cacetttece actgaececa taaaggaate etcatggeca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attottgaat gagtootata aacatgaaca ggtttatatt cgaagcacag 360
acqttqaccq qactttgatg aagtgctatg acaaacctgg caagcccg
3 35 35 55 66 36 3
<220>
<221> misc_feature
<222> (1)...(352)
\langle 223 \rangle n = A,T,C or G
<400> 421
gctcaaaaat ctttttactg atnggcatgg ctacacaatc attgactatt acggaggcca 60
gaggagaatg aggcctggcc tgggagccct gtgcctacta naagcacatt agattatcca 120
ttcactgaca gaacaggtct tttttgggtc cttcttctcc accacnatat acttgcagtc 180
ctccttcttg aagattcttt ggcagttgtc tttgtcataa cccacaggtg tagaaacaag 240
ggtgcaacat gaaatttctg tttcgtagca agtgcatgtc tcacaagttg gcangtctgc 300
cactccgagt ttattgggtg tttgtttcct ttgagatcca tgcatttcct gg
a<210> 422 ಸಂಪೂರ್ವರಗಳು ಸಾರ್ಥಿಸಿಕ ಚಿತ್ರಕ್ಕಾರಿಗಳು
<211> 337 Tgd.m. guget [280 (vip (m. print) large large mediant) [290 (vip (p. l.) ] ];
្គី<212> DNA ប៉ាន់ទៅការមួយពេញ ពេលមានបទពេលគេ ពេលប្រាស់ សមុខ្លាស់ ខេត្ត នៅការគេ បានប្រាស់បាន
ស្សាស្សាស្ថិត និងបាន ស្វែង
<400> 422
atgccaccat gctggcaatg cagcgggcgg tcgaaggcct gcatatccag cccaagctgg 60
cgatgatcga cggcaaccgt tgcccgaagt tgccgatgcc agccgaagcg gtggtcaagg 120
gegatageaa ggtgccggcg atcgcggcgg cgtcaatect ggccaaggtc agccgtgatc 180
gtgaaatggc agctgtcgaa ttgatctacc cgggttatgg catcggcggg cataagggct 2403
atecgacace ggtgcacetg gaageettge ageggetggg geegaegeeg atteacegae 300%
gettetteeg eeggtaegge tggeetatga aaattat
```

```
<210> 423
<211> 310
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(310)
<223> n = A, T, C or G
<400> 423
gctcaaaaat ctttttactg atatggcatg gctacacaat cattgactat tagaggccag 60
aggagaatga ggcctggcct gggagccctg tgcctactan aagcncatta gattatccat 120
tcactgatag aacaggtett ttttgggtee ttetteteea ccaegatata ettgeagtee 180
teettettga agattetttg geagtigtet ttgteataac ceacaggtgt anaaacaagg 240
gtgcaacatg aaatttctgt ttcgtagcaa gtgcatgtct cacagttgtc aagtctgccc 300
tecgagttta
<210> 424
<211>, 370
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(370)
<223> n = A, T, C or G
<400> 424
gctcaaaaat ctttttactg ataggcatgg ctacacaatc attgactatt agaggccaga 60
ggagaatgag gcctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120
cactgacaga acaggtettt tttgggteet tetteteeac cacgatatae ttgeagteet 180
cettettgaa gattetttgg cagttgtett tgteataace cacaggtgta gaaacateet 240
ggttgaatct cctggaactc cctcattagg tatgaaatag catgatgcat tgcataaagt 300
cacgaaggtg gcaaagatca caacgctgcc cagganaaca ttcattqtga taagcaggac 360
tccgtcgacg
<210> 425
<211> 216
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(216)
                                in the state of the property of the contract of the second
<223> n = A, T, C or G
                            aattgctatn ntttattttg ccactcaaaa taattaccaa aaaaaaaaa tnttaaatga 60
taacaacnca acatcaaggn aaananaaca ggaatggntg actntgcata aatnggccga 120
anattateca ttatnttaag ggttgaette aggntacage acacagacaa acatgeecag 180
gaggntntca ggaccgctcg atgtnttntg aggagg
                                                               216
                                      that it is strong to the spage of the
<210> 426
<211> 596'
<212> DNA
<213> Homo sapiens
```

Billedgen code (C.E.)

```
cttccagtga ggataaccct gttgccccgg gccgaggttc tccattaggc tctgattgat 60
 tggcagtcag tgatggaagg gtgttetgat catteegact geeceaaggg tegetggeea 120
 gctctctgtt ttgctgagtt ggcagtagga cctaatttgt taattaagag tagatggtga 180
  gctgtccttg tattttgatt aacctaatgg ccttcccagc acgactcgga ttcagctgga 240
  gacatcacgg caacttttaa tgaaatgatt tgaagggcca ttaagaggca cttcccgtta 300
 ttaggcagtt catctgcact gataacttct tggcagctga gctggtcgga gctgtggccc 360
 aaacgcacac ttggcttttg gttttgagat acaactctta atcttttagt catgcttgag 420
  ggtggatgge etttteaget ttaacceaat ttgcactgee ttggaagtgt agceaggaga 480
 atacacteat atactegtgg gettagagge cacageagat gteattggte tactgeetga 540
 gtcccgctgg tcccatccca ggaccttcca tcggcgagta cctgggagcc cgtgct
                               The set I have to
 <210> 427
<211> 107
<212> DNA
<213> Homo sanions
 <210> 427
<213> Homo sapiens
 <220>
 <221> misc feature
 <222> (1)...(107)
 <223> n = A, T, C or G
 gaagaattca agttaggttt attcaaaggg cttacngaga atcctanacc caggncccag 60
 cccgggagca gccttanaga gctcctgttt gactgcccgg ctcagng
 <210> 428
 <211> 38
 <212> DNA
 <213> Homo sapiens
                                            7. 3
                                    and the state of t
                                                                                          <220>
                                                                                           Critical Section
 <221> misc_feature
                                                                    and the first of the
 <222> (1) ... (38)
                                                                      o o o egymente de la propieta de la companya de la
La companya de la co
 <223> n = A, T, C or G
 <400> 428
 gaacttccna anaangactt tattcactat tttacatt
                                                                                                                                           38
 <210> 429
 <211> 544
 <212> DNA
 <213> Homo sapiens
 <400> 429
 ctttgctgga cggaataaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60
 attgaagage ggetgeagee etgeggttea gattaaaate egagaattgt atagaegeeg 120
atatccacga actcttgaag gactttctga tttatccaca atcaaatcat cggttttcag 180
tttggatggt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactcgtt 240
geettecaet teagttacae etcaeteaec atecteteet gttggttetg tgetgettea 300
agatactaag cccacatttg agatgcagca gccatctccc ccaattcctc ctgtccatcc 360
agatactaag cccacatttg agatgcaya gourtous gatgtctta tcaagcccac 420 tgatgtgcag ttaaaaaatc tgcccttta tgatgtcctt gatgttctca tcaagcccac 420
gagtttagtt caaagcagta ttcagcgatt tcaagagaag ttttttattt ttgctttgac 480
acctcaacaa gttagagaga tatgcatatc cagggatttt ttgccaggtg gtaggagaga 540
ttat
                                                                                                                                                 . . < 6.53
                                                                                                                                            1 15 8368
```

<210> 430

```
<211> 507
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(507)
\langle 223 \rangle n = A, T, C or G
<400> 430
cttatcncaa tggggctccc aaacttggct gtgcagtgga aactccgggg gaattttgaa 60
gaacactgac acceatette caccegaca etetgattta attgggetge agtgagaaca 120
gagcatcaat ttaaaaagct gcccagaatg ttntcctggg cagcgttgtg atctttgccn 180
cettegtgae tttatgeaat geateatget attteatace taatgaggga gtteeaggag 240
atteaactag gatgttteta encetgtggg ttatgacaaa gacaactgee aaagaatntt 300
caagaaggag gactgcaagt atatcgtggt ggagaagaag gacccaaaaa agacctgttc 360
tgtcagtgaa tggataatct aatgtgcttc tagtaggcac agggctccca ggccaggcct 420
cattetecte tggcetetaa tagteaatga ttgtgtagee atgeetatea gtaaaaagat 480
ttttgagcaa aaaaaaaaa aaaaaaa
                                                                 507
<210>, 431
<211> 392
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(392)
<223> n = A, T, C or G
<400> 431
gaaaattcag aatggataaa aacaaatgaa gtacaaaata tttcagattt acatagcgat 60
aaacaagaaa gcacttatca ggaggactta caaatggaag tacactctan aaccatcatc 120
tatcatggct aaatgtgaga ttagcacagc tgtattattt gtacattgca aacacctaga 180
aagagatggg aaacaaaatc ccaggagttt tgtgtgtgga gtcctgggtt ttccaacaga 240
catcattcca gcattctgag attagggnga ttggggatca ttctggagtt ggaatgttca 300
acaaaagtga tgttgttagg taaaatgtac aacttctgga tctatgcaga cattgaaggt 360
gcaatgagtc tggcttttac tctgctgttt ct
                                                                 392
<210> 432
<211> 387
<212> DNA
                                <213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(387)
<223> n = A, T, C or G
<400> 432
ggtatccnta cataatcaaa tatagctgta gtacatgttt tcattggngt agattaccac 60
aaatgcaagg caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg 120
ngtagtecaa geteteggna gtecageeae tgngaaacat getecettta qattaacete 180
gtggacnetn ttgttgnatt gtetgaactg tagngeeetg tattttgett etgtetgnga 240
attetgttgc ttetggggca ttteettgng atgeagagga ceaceaeaa gatgaeagea 300
atctgaattg ntccaatcac agctgcgatt aagacatact gaaatcgtac aggaccggga 360
acaacgtata gaacactgga gtccttt
                                                                 387
```

```
<210> 433
<211> 281
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(281)
<223> n = A, T, C or G
<400> 433
ttcaactage anagaanact gettcagggn gtgtaaaatg aaaggettee aegeagttat 60
ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120
caggenetat ttgggttgge tggaggaget gtggaaaaca tggagagatt ggegetggag 180
ategeegtgg etatteeten ttgntattae accagngagg ntetetgtnt geeeactggt 240
tnnaaaaccg ntatacaata atgatagaat aggacacaca t 200 200 201
          ကားသွားများသည်။ ကာလေးလုံးမှုမှုနှာ မောက်သွားမျိုးနှာကြောင့် ကွေ့ဘုရာ ၉ မည်မှ မြောင့်မှု
<211> 484
                                           14.0 × 1 × 1 × 1 × 2. ×
<212> DNA
<213> Homo sapiens
<400> 434
ttttaaaata agcatttagt gctcagtccc tactgagtac tctttctctc ccctcctctg 60
aatttaattc tttcaacttg caatttgcaa ggattacaca tttcactgtg atgtatattg 120
tgttgcaaaa aaaaaaaagt gtctttgttt aaaattactt ggtttgtgaa tccatcttgc 180
tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240
agctagtcta tcagcatctg acaggtgaat tggatggttc tcagaaccat ttcacccaga 300
cagoctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca taacaaaccc 360
tgctccaatc tgtcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420
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               <210> 435
<211> 424
<212> DNA
<213> Homo sapiens
<400> 435
gegeegetea gageaggtea etttetgeet teeaegteet cetteaagga ageeceatgt 60:
gggtagettt caatategea ggttettaet eetetgeete tataagetea aacceaceaa 120 -
cgatcgggca agtaaacccc ctccctcgcc gacttcggaa ctggcgagag ttcagcgcag 180
atgggcctgt ggggaggggg caagatagat gagggggagc ggcatggtgc ggggtgaccc 240
cttggagaga ggaaaaaggc cacaagaggg gctgccaccg ccactaacgg agatggccct 300
ggtagagacc tttgggggtc tggaacctct ggactcccca tgctctaact cccacactct 360
gctatcagaa acttaaactt gaggattttc tctgtttttc actcgcaata aattcagagc 420
                                                         424
aaac
<210> 436
<211> 667
<212> DNA
                    ्रमृत्यु कृष्टि व्यक्ष में प्रदूषण अक्षम् करम्बन्धा हुव क्षम् अ<mark>रुव्यम्</mark> । स्वर्णा कर्षे कर्णाणा क
<213> Homo sapiens
                    o a distribución por ma en la registada o como go de regio a exposación de que como el cual que
<220>
                     in gradice in principagana in petros visity in a regardic incumosopal,
<223> n = A, T, C or G
                                           ាឌីស្រា ញែ ខ្លួនបាននេះ ស្រែងសេស 🗀
```

```
<400> 436
accttgggaa nactctcaca atataaaggg tcgtagactt tactccaaaat tccaaaaagg 60
tcctggccat gtaatcctga aagttttccc aaggtagcta taaaatcctt ataagggtgc 120
agoctottot ggaattooto tgatttoaaa gtotoactot caagttottg aaaacgaggg 180
caqttcctqa aaqqcaqqta taqcaactga tcttcaqaaa gaggaactgt gtgcaccggg 240
atgggctgcc agagtaggat aggattccag atgctgacac cttctggggg aaacagggct 300
gccaggtttg tcatagcact catcaaagtc cggtcaacgt ctgtgcttcg aatataaacc 360
tgttcatgtt tataggactc attcaagaat tttctatatc tctttcttat atactctcca 420
agttcataat gctgctccat gcccagctgg gtgagttggc caaatccttg tggccatgag 480
gattccttta tggggtcagt gggaaaggtg tcaatgggac ttcggtctcc atgccgaaac 540
accaaaqtca caaacttcaa ctccttqqct agtacacttc ggtctagcca gaaaaaaaagc 600
agaaacaaga agccaaggct aaggcttgct gccctgccag gaggaggggt gcagctctca 660
tqttqaq
                                grand the case of cases of the second of the second
<210> 437
<210> 437
<211> 693
<212> DNA
<213> Homo sapiens
                         Some the engal of the control of the
<400> 437
ctacgtctca accetcattt ttaggtaagg aatettaagt ccaaagatat taagtgacte 60
acacagccag gtaaggaaag ctggattggc acactaggac tctaccatac cgggttttgt 120
taaagctcag gttaggaggc tgataagctt ggaaggaact tcagacagct ttttcagatc 180
ataaaaqata attettagee catgttette teeagageag acetgaaatg acageacage 240
aggtactect etatttteac ecetettget tetactetet ggeagteaga eetgtgggag 300
qccatqqqaq aaaqcagctc tctggatgtt tgtacagatc atggactatt ctctgtggac 360
catttctcca ggttacccta ggtgtcacta ttggggggac agccagcatc tttagctttc 420
atttgagttt ctgtctgtct tcagtagagg aaacttttgc tcttcacact tcacatctga 480
acacctaact gctgttgctc ctgaggtggt gaaagacaga tatagagctt acagtattta 540
tectattet aggeactgag ggetgtgggg tacettgtgg tgccaaaaca gateetgttt 600
taaggacatg ttgcttcaga gatgtctgta actatctggg ggctctgttg gctctttacc 660
ctgcatcatg tgctctcttg gctgaaaatg acc
                                                                                                                      693
<210> 438
<210> 438
<211> 360
<212> DNA
<212> DNA
<213> Homo sapiens
<400> 438
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ttatgcaatg catcatgcta tttcatacct aatgagggag ttccaggaga ttcaaccagg 120
atgtttctac acctgtgggt tatgacaaag acaactgcca aagaatcttc aagaaggagg 180
actgcaagta tatctggtgg agaagaagga cccaaaaaag acctgttctg tcagtgaatg 240'
qataatctaa tqtqcttcta gtaggcacag ggctcccagg ccaggcctca ttctcctctg 300
gcctctaata gtcaataatt gtgtagccat gcctatcagt aaaaagattt ttgagcaaac 360
<210> 439
                                                                      n de la companya de l
<211> 431
<212> DNA
                                                                 <213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(431)
<223> n = A, T, C or G
<400> 439
qttcctnnta actcctqcca qaaacagctc tcctcaacat gagagctqca cccctcctcc 60
```

```
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gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacetttece actgacecca taaaggaate etcatggeca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attottgaat gagtootata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
aegttgaceg gactttgatg agtgetatga caaacetgge agecegtega egeggeegeg 420
431

<210> 440
<211> 523
<212> DNA
<213> Homo sapiens
<400> 440
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tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttacccat cagttccagc 240
cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agttttctcc 300
actggaaaac tgctactatc tgtttttata tttctgttaa aatatatgag gctacagaac 360
taaaaattaa aacctctttg tgtcccttgg tcctggaaca tttatgttcc ttttaaagaa 420
acaaaaatca aactttacag aaagatttga tgtatgtaat acatatagca gctcttgaag 480
tatatatatc atagcaaata agtcatctga tgagaacaag cta 523

<210> 441
<211> 430
<212> DNA
<213> Homo sapiens
<400> 441

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gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attottgaat gagtootata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
aatttagtag
                                                                 430
<210> 442

<211> 362

<212> DNA

<213> Homo sapiens
ctaaggaatt agtagtgttc ccatcacttg tttggagtgt gctattctaa aagattttga 60
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cttcacttct gatacttgta aattaatctt ttattgcact tgttttgacc attaagctat 180
atgtttagaa atggtcattt tacggaaaaa ttagaaaaat tctgataata qtqcaqaata 240
aatgaattaa tyttttactt aatttatatt gaactgtcaa tgacaaataa aaattctttt 300
tgattatttt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360
tc
                                                                 362
<210> 443
<211> 624
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<222> (1)...(624)
<223> n = A,T,C or G
<400> 443
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ttgaaagaat taaattcaga ggaggggaga gaaagagtac tcagtaggga ctgagcacta 120
aatgcttatt ttaaaagaaa tgtaaagagc agaaagcaat tcaggctacc ctgccttttg 180
tgctggctag tactccggtc ggtgtcagca gcacgtggca ttgaacattg caatgtggag 240
cccaaaccac agaaaatggg gtgaaattgg ccaactttct attaacttgg cttcctgttt 300
tataaaatat tgtgaataat atcacctact tcaaagggca gttatgaggc ttaaatgaac 360
taacgcctac aaaacactta aacatagata acataggtgc aagtactatg tatctggtac 420
atggtaaaca toottattat taaagtoaac gotaaaatga atgtgtgtgc atatgctaat 480
agtacagaga gagggcactt aaaccaacta agggcctgga gggaaggttt cctggaaaga 540
ngatgcttgt gctgggtcca aatcttggtc tactatgacc ttggccaaat tatttaaact 600
ttgtccctat ctgctaaaca gatc

<210> 444

<211> 425
<211> 425
                                         ...
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(425)
<223> n = A, T, C or G
<400> 444
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gaagetttgt ccaggeetgt gtgtgaacce aatgttttge ttagaaatag aacaagtaag 120
ttcattgcta tagcataaca caaaatttgc ataagtggtg gtcagcaaat ccttgaatgc 180
tgcttaatgt gagaggttgg taaaatcctt tgtgcaacac tctaactccc tgaatgtttt 240
getgtgetgg gacetgtgca tgccagacaa ggccaagetg getgaaagag caaccageca 300
cctctgcaat ctgccacctc ctgctggcag gatttgttt tgcatcctgt gaagagccaa 360
ggaggcacca gggcataagt gagtagactt atggtcgacg cggccgcgaa tttagtagta 420
                     425
gtaga
<210> 445
<211> 414
<212> DNA
                         <213> Homo sapiens
<220>
<221> misc feature
                                                                38 KUIS
<222> (1)...(414)
                                                                \{a,b,b,c,c,b\}
<223> n = A, T, C \text{ or } G
                                                        Electrical and proceedings.
<400> 445
catgtttatg nttttggatt actttgggca cctagtgttt ctaaatcgtc tatcattctt 60
ttctgttttt caaaagcaga gatggccaga gtctcaacaa actgtatctt caagtctttg 120
tgaaattett tgeatgtgge agattattgg atgtagttte etttaactag catataaate 180
tggtgtgttt cagataaatg aacagcaaaa tgtggtggaa ttaccatttg gaacattgtg 240
aatgaaaaat tgtgtctcta gattatgtaa caaataacta tttcctaacc attgatcttt 300
ggatttttat aatcctactc acaaatgact aggcttctcc tcttgtattt tgaagcagtg 360
tgggtgctgg attgataaaa aaaaaaaaag tcgacgcggc cgcgaattta gtag
```

\* 1 1 × 3 1 1

```
<211> 631
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(631)
e in the
                                                           Particle Carrier Configuration on Marketine (1)
acaaattaga anaaagtgcc agagaacacc acataccttg teeggaacat tacaatggct 60
totgcatgca tgggaagtgt gagcattota tcaatatgca ggagccatct tgcaggtgtg 120
atgctggtta tactggacaa cactgtgaaa aaaaggacta cagtgttcta tacgttgttc 180
coggtoctgt acgatttcag tatgtottaa togcagotgt gattggaaca attcagattg 240
ctgtcatctg tgtggtggtc ctctgcatca caagggccaa actttaggta atagcattgg 300
actgagattt gtaaactttc caacettcca ggaaatgeec cagaagcaac agaattcaca 360 gacagaagca aaatacaggg cactacagtt cagacaatac aacaagagcg tccacgaggt 420
taatctaaag ggagcatgtt tcacagtggc tggactaccg agagcttgga ctacacaata 480
cagtattata gacaaaagaa taagacaaga gatctacaca tgttgccttg catttgtggt 540
aatctacacc aatgaaaaca tgtactacag ctatatttga ttatgtatgg atatatttga 600
                                                                                                                        631
aataqtatac attqtcttga tqttttttct q
                                                                                                                          Sec. 1993 453
<210> 447
<211> 585
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(585)
<223> n = A,T,C or G . A substituting the parameter A and A are the parameter A are the parameter A and A are the parameter A are the parameter A are the parameter A are the parameter A and A are the parameter A and A are the parameter A are the paramet
ccttgggaaa anthtcacaa tataaagggt cgtagacttt actccaaatt ccaaaaaggt 60
cctggccatg taatcctgaa agttttccca aggtagctat aaaatcctta taagggtgca 120
geetettetg gaatteetet gattteaaag teteaetete aagttettga aaacgaggge 180
agttcctgaa aggcaggtat agcaactgat cttcagaaag aggaactgtg tgcaccggga 240
tgggctgcca gagtaggata ggattccaga tgctgacacc ttctggggga aacagggctg 300
ccaggtttgt catagcactc atcaaagtcc ggtcaacgtc tgtgcttcga atataaacct 360
gttcatgttt ataggactca ttcaagaatt ttctatatct ctttcttata tactctccaa 420
gttcataatg ctgctccatg cccagctggg tgagttggcc aaatccttgt ggccatgagg 480
attectttat ggggteagtg ggaaaggtgt caatgggaet teggteteea tgeegaaaca 540
ccaaagtcac aaacttcaac teettggeta gtacactteg gteta
<210> 448
<211> 93
<212> DNA
<213> Homo sapiens
<220>
ာက္ေတြ မွာ မို႕တီလက္ လူလည္း အေရာက္အတြင္းမွာ ကို မြန္မေတြကို အေတြကို မို႕လည္း လူလည္း လူလည္း လူလည္း
အေရာက္ေတြကို လူလည္း အေလာက္ေတြကို လူလည္း ေတြကို လည္းေတြကို လည္းေတြကို လည္းေတြကို လည္းသည္။ လည္းလည္း လည္းလည္း လွ
tgctcgtggg tcattctgan nnccgaactg accntgccag ccctgccgan gggccnccat 60
ggctccctag tgccctggag agganggggc tag with the state of the game 93 to the
```

```
<210> 449
<211> 706
<212> DNA
<213> Homo sapiens 🗽
<220>
<221> misc feature
<222> (1) ... (706)
<223> n = A, T, C or G
<400> 449
ccaagttcat gctntgtgct ggacgctgga cagggggcaa aagcnnttgc tcgtgggtca 60
ttctgancac cgaactgacc atgccagccc tgccgatggt cctccatggc tccctagtgc 120
cctggagagg aggtgtctag tcagagagta gtcctggaag gtggcctctg ngaggagcca 180
cggggacage atectgcaga tggtegggeg egteceatte gecatteagg etgegeaact 240
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cgacggccag tgaattgaat ttaggtgacn ctatagaaga gctatgacgt cgcatgcacg 420
cgtacgtaag cttggatcct ctagagcggc cgcctactac tactaaattc gcggccgcgt 480
cgacgtggga tccncactga gagagtggag agtgacatgt gctggacnct gtccatgaag 540
cactgagcag aagctggagg cacaacgcnc cagacactca cagctactca ggaggctgag 600
aacaggttga acctgggagg tggaggttgc aatgagctga gatcaggccn ctgcncccca 660
gcatggatga cagagtgaaa ctdcatctta aaaaaaaaaa aaaaaa
                                                                706
<210> 450
<211> 493
<212> DNA
<212> DNA
<213> Homo sapiens
<400> 450
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acagttttaa aaggtaaaac aacataaaaa gaaatatcct atagtggaaa taagagagtc 120
aaatgagget gagaacttta caaagggate ttacagacat gtegecaata teactgeatq 180
agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga qqtacaattc 240
caagtcaggt agtgaaatgg gtggaattaa actcaaatta atcctgccag ctgaaacgca 300
agagacactg tcagagagtt aaaaagtgag ttctatccat gaggtgattc cacagtcttc 360
tcaagtcaac acatctgtga actcacagac caagttctta aaccactgtt caaactctgc 420
tacacatcag aatcacctgg agagetttac aaacteccat tgeegagggt egacgeggec 480
gcgaatttag tag
                                                                493
<210> 451
<211> 501
<212> DNA
<213> Homo sapiens
<220>
                                                                 188 6
<221> misc feature
<222> (1)...(501)
                                                        the trace was production
<223> n = A, T, C or G
<400> 451
gggcgcgtcc cattcgccat tcaggctgcg caactgttgg gaagggcgat cggtgcgggc 60
ctcttcgcta ttacgccagc tggcgaaagg gggatgtgct gcaaggcgat taagttgggt 120
aacgccaggg ttttcccagt cncgacgttg taaaacgacg gccagtgaat tgaatttagg 180
tgacnctata gaagagctat gacgtcgcat gcacgcgtac gtaagcttgg atcctctaga 240
geggeegeet actactacta aattegegge egegtegaeg tgggateene actgagagag 300
tggagagtga catgtgctgg acnetgteca tgaagcactg agcagaaget ggaggcacaa 360
cgcnccagac actcacagct actcaggagg ctgagaacag gttgaacctg ggaggtggag 420
```

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```
qttqcaatqa qctqaqatca qgccnctqcn ccccaqcatq gatqacagag tgaaactcca 480
                                                                                                                                                                                                                 501
 tcttaaaaaa aaaaaaaaaa a
 <210> 452
 <211> 51
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc feature
 <222> (1)...(51)
 <223> n = A, T, C or G
                                  tuak pari bila b
 <400> 452
agacggtttc accnttacaa cnccttttag gatgggnntt ggggagcaag c
<2.13> Homo sapiens
*** The part of the part
The confidence of the confiden
 <222> (1)...(317)
 <223> n = A,T,C or G
 <400> 453
 tacatettge ttttteecea ttggaactag teattaacee atetetgaae tggtagaaaa 60°
 acatetgaag agetagteta teageatetg geaagtgaat tggatggtte teagaaceat 120
 ttcacccana cagcctqttt ctatcctqtt taataaatta gtttgqqttc tctacatqca 180
 taacaaaccc tgctccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240
 cccaccaaac tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300
                                                                                            ente de la filipa d
La filipa de la fil
 tacccatgtc tttatta
                                   4 4 4 4 4
                                                                                                       and our last of
 <210> 454
<211> 231
<212> DNA
                                                                                             <213> Homo sapiens
                      , the first of the second second
 <400> 454
 ttcgaggtac aatcaactct cagagtgtag tttccttcta tagatgagtc agcattaata 60
 taagccacge cacgetettg aaggagtett gaatteteet etgeteacte agtagaacea 120
 agaagaccaa attettetge atcecagett geaaacaaaa ttgttettet aggteteeae 180
 ccttcctttt tcagtgttcc aaagctcctc acaatttcat gaacaacagc t
                                                                                                                                                                                                                231
<210> 455
 <211> 231
 <212> DNA
<213> Homo sapiens
 <400> 455
taccaaagag ggcataataa tcagtctcac agtagggttc accatcctcc aagtgaaaaa 60
cattettece aategeettt ccacageeta cacacacaa acaggaaaca teccaagett 120
gtttcaacgc attgatgact tetecaagga tetteetttg gcategacca catteagggg 180
ာ ၂၈၈၂ ၂၂ ၁၈၂၅ ပုဂ္ဂန္ကာရန္ က အေက ပုဂ္ဂန္ရက္မွာ မဆင္ဆည္းသူ မေတြ ဥပေဒတ္ လွေးအတြဲ လွေးကြမည္မတည့္
<211> 231
                                                                      ការប្រសិទ្ធភាព ខ្លាំង ការប្រសិទ្ធភាព ការប្រជាធាតិបាន ស្ថានភាពប្រជ័ន្ធនាការប្រជាធាតិបាន ប
```

| <212> DNA   | ١.,                                   |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
|-------------|---------------------------------------|----------------------|---------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|-----------|
| <213> Homo  | esniene '                             |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| ~21J/ HOMO  | gabrens                               |                      | 1                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
|             |                                       | 1                    |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| <400> 456   |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| ttggcaggta  | cccttacaaa                            | gaagacacca           | taccttatac                            | gttattaggt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | ggaataatca       | 60        |
| ttccattcac  | tattatcgtt                            | attattette           | nanaaaccct                            | atctatttac                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | totaacettt       | 120       |
|             |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
|             | ttcctttatc                            |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| cctttttatt  | tggtgcagct                            | gctagtcagt           | ccctgactga                            | cattgccaag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | t                | 231       |
|             |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | ,                |           |
| <210> 457   |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  | ٠.        |
| <211> 231   | *                                     |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | •• '             |           |
|             |                                       |                      | •                                     | 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 4                |           |
| <212> DNA   | *                                     |                      | 1                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| <213> Homo  | sapiens                               |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
|             | +                                     | 1                    |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| <220> ►     | i                                     | 1                    |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
|             |                                       | :                    |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| <221> misc  |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| <222> (1).  |                                       | ,                    |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| <223> n = . | A,T,C or G                            |                      |                                       | •                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                  |           |
| • • • •     | 1 1.7                                 |                      | •                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  | ·         |
| <400> 457   |                                       | in the second second |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
|             |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
|             | aggggtctga                            |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| gcattcctta  | atatgatctt                            | gctataatta           | gatttttctc                            | cattagagtt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | catacagttt       | 120       |
| tatttgattt  | tattagcaat                            | ctctttcaga           | agacccttga                            | gatcattaag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | ctttgtatcc       | 180       |
|             | atcgatgcct                            |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  | 231       |
| ageegeeeda  | accyacyce                             | Caccccccc            | gaggegeege                            | cygococogo                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 9                | 231       |
| .010. (20   |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| <210> 458   |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| <211> 231   |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | •                |           |
| <212> DNA   | •                                     |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | • .              |           |
| (213> Homo  | sapiens                               |                      |                                       | 5.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                  | _         |
| JETON HOTIO | Saprens                               |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
|             |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | •                |           |
| <400> 458   |                                       |                      |                                       | · : · · · · · · · · · · · · · · · · · ·                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                  | 1         |
| aggtctggtt  | cccccactt                             | ccactcccct           | ctactctctc                            | taggactggg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | ctgggccaag       | 60        |
|             | tggttaggga                            |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
|             | cttgggtaac                            |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
|             |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| ggtactgggt  | taggcatttt                            | ggggggccag           | accccaggag                            | aagaagattc                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | τ                | 231       |
|             |                                       | 4                    |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| <210> 459   |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  | -         |
| <211> 231   |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | •                |           |
| <212> DNA   |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
|             |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| <213> Homo  | sapiens                               |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| 4.5         |                                       |                      | 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  | ٠.٠٠.     |
| <400> 459   |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | And the state of |           |
|             | ctcgctgaca                            | сададаласс           | ccaacacaaa                            | gaaaggaatg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | decadecaea       | 60        |
| 77          | acctgtggtg                            |                      | antone                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  | 100       |
|             |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
|             | gttttccctc                            |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| actatacaca  | gtcaccgtcc                            | caatgagaaa           | caagaaggag                            | caccetccac                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | a                | 231       |
|             | -                                     |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| 210> 460    |                                       | •                    |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | # # 155.2        |           |
|             |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  | 1 - 1 - 1 |
| 211> 231    |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| <212> DNA   |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  | :.·       |
| 213> Homo   | sapiens                               | 1                    | ad tid Lisa iztatili.                 | Linds to protect the control of the | r . **           |           |
|             | · · · · · · · · · · · · · · · · · · · | 131                  |                                       | getan eelis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                  |           |
| 100> 460    |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| 400/ 400    |                                       |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  | 10.00     |
|             | catgctgcaa                            |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| ctatcaccc   | tattcttggg                            | ggctgcttct           | tcacagtgat                            | catgaagcct                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | agcagcaaat       | 120       |
|             | cacacgcaca                            |                      |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                  |           |
| tagaactta   | gtccagcctc                            | cartecacce           | ctaccacact                            | taaggataga                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                  | 231       |
| ,           |                                       |                      | uayyuu                                | -uuyya caya                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | u                |           |

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<210> 461
<211> 231
<212> DNA
<213> Homo sapiens
                                                  Library Construction may report on
<400> 461
cgaggtttga gaagctctaa tgtgcagggg agccgagaag caggcggcct agggagggtc 60
gcgtgtgctc cagaagagtg tgtgcatgcc agaggggaaa caggcgcctg tgtgtcctgg 120
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<211> 231
<212> DNA
<213> Homo sapiens
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totagaggag gtatttaatt tottotoact catocagtgt tgtatttagg a 231
<212> DNA
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| <210> 477<br><211> 140<br><212> PRT<br><213> Homo sapiens                                                                                                                                                                        |                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | in the second                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| <400> 477 Met Asp+Gly His Thr Asp Ile Trr 5'                                                                                                                                                                                     | Arg Asn His                                                                                                    | Met Asp Thr Pro Pro<br>15                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| His Tyr His Arg Asp Thr Asp Thr<br>20                                                                                                                                                                                            | Arg Arg His                                                                                                    | His His Met Asp Thr<br>30                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | <b>.</b> (1.4)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Leu Ser His Tyr His Arg Asp Thr<br>35 40                                                                                                                                                                                         |                                                                                                                | Thr Val Thr Trp Thr<br>45                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| His His His Thr His Glu His Thr                                                                                                                                                                                                  |                                                                                                                | Pro Tyr Gly His Trp<br>60                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| His Thr His Cys His Thr Val Thr<br>65 70                                                                                                                                                                                         | r Trp Thr His<br>75                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | en e                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Pro Pro His Thr Leu Pro Val Asp<br>85                                                                                                                                                                                            | o Thr Arg Thr<br>90                                                                                            | His Arg His Cys His<br>95                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Thr Asp Thr Gln Asn Thr Val Thr<br>100                                                                                                                                                                                           | r Arg Arg His<br>105                                                                                           | His His Ala Asp Thr                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Pro Pro Leu Trp Cys Arg Leu Asr<br>115 120                                                                                                                                                                                       |                                                                                                                | Gly Gly Thr Ala Val<br>125                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Ala Tyr Ser Cys Leu Ser Asp Trp<br>130 135                                                                                                                                                                                       | o Leu Ser Pro                                                                                                  | Gln<br>140                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <210> 478<br><211> 143<br><212> PRT                                                                                                                                                                                              | ar en en en er |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | ngMana Alles Andi<br>ng                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|                                                                                                                                                                                                                                  | Sea Sea Sea                                                                                                    | $\frac{(k_1,k_2,k_3)}{(k_1,k_2)} \leq \frac{(k_1,k_2)}{(k_1,k_3)} \leq \frac{(k_1,k_3)}{(k_1,k_3)} \leq \frac{(k_1,k_3)}$ | under transfordische<br>Et                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| <400> 478 Met Tyr Arg Ris Thr Glu Thr Leu 5                                                                                                                                                                                      | Pro His Gly                                                                                                    | Asp Thr Val Thr Gln 15                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 2000 - 200 - 200<br>Carlo                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| Ser His Gly His Thr Gly Ile Val                                                                                                                                                                                                  | l Thr Trp Thr<br>25                                                                                            | Asp Thr Gln Thr Tyr                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Gly Glu Ile Thr Trp Thr His His 35                                                                                                                                                                                               |                                                                                                                | Thr Gly Thr Gln Thr                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | e de la companya de l |
| His Gly Asp Ile Thr Thr Trp Thr                                                                                                                                                                                                  | r His Cys His                                                                                                  | Thr Thr Gly Thr                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |

| 50.                                 | • ,               | 55                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | •                  | <b>60</b> ° # 40 ± 5                                                                                                                                                                                                                                                                                                                                |                        |
|-------------------------------------|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|
| Arg Asp Ile 3                       | Thr Leu S         | 70 / // // //                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | His Thr Ile        | Thr His Met Asn                                                                                                                                                                                                                                                                                                                                     | <b>80</b> %            |
| -Pro Thr His (                      | Cys His M         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | · ·                | Thr Ala Thr Leu<br>95                                                                                                                                                                                                                                                                                                                               |                        |
| _                                   | Thr Ser Ti<br>100 | nr Pro Ser                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | His His His<br>105 | Thr His Cys Leu<br>110                                                                                                                                                                                                                                                                                                                              | Trp                    |
| Thr Gln Gly I                       | His Thr A         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                    | His Lys Thr Leu<br>125                                                                                                                                                                                                                                                                                                                              | <b>Ser</b> 43 70 - 675 |
| His Gly Asp 1                       | * - 1.            | 135                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 1                  | 140                                                                                                                                                                                                                                                                                                                                                 | short free o           |
| <210> 479<br><211> 222<br><212> PRT |                   | and the distance of the distan | •                  | Salara Juliana da Parangan Pangan Pangan<br>Pangan Pangan Panga<br>Pangan Pangan | grating to the second  |
| <213> Homo sa                       | apiens            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                    |                                                                                                                                                                                                                                                                                                                                                     |                        |
|                                     | His Thr G         | lu Thr Leu                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Pro His Gly<br>10  | Asp Thr Val Thr                                                                                                                                                                                                                                                                                                                                     | Gln                    |
| Ser His Glu H                       | His Thr G<br>20   | ly Ile Val                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Thr Trp Thr<br>25  | Asp Thr Gln Thr                                                                                                                                                                                                                                                                                                                                     | Tyr                    |
| Gly Glu Ile 3                       |                   | nr His His<br>40                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | His Thr Ile        | Thr Gly Thr Gln<br>45                                                                                                                                                                                                                                                                                                                               | Thr                    |
| His Gly Asp 3                       |                   | nr Trp Thr<br>,55                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | His Cys His        | Thr Thr Thr Gly                                                                                                                                                                                                                                                                                                                                     | Thr **                 |
| Arg Asp Ile 3                       | Thr Leu S         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                    | Thr His Met Asn                                                                                                                                                                                                                                                                                                                                     | Thr<br>80              |
| Pro Thr His (                       | Cys His Mo<br>85  | et Asp Thr                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Ala Thr His        | Thr Ala Thr Leu<br>95                                                                                                                                                                                                                                                                                                                               | Ser                    |
|                                     | Thr Ser I<br>100  | le Pro Ser                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | His His His<br>105 | Thr His Cys His<br>110                                                                                                                                                                                                                                                                                                                              | Val                    |
| Asp Thr Arg 1                       | Thr His A         | rg His Cys<br>120                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                    | Thr Gln Asn Thr<br>125                                                                                                                                                                                                                                                                                                                              | Val                    |
| Thr Arg Arg H                       | His His H         | is Ala Asp<br>135                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Thr Pro Pro        | His Gly His Ser<br>140                                                                                                                                                                                                                                                                                                                              | Thr                    |
| Arg His Ser A                       | •                 | ln Ile His<br>50                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | His His Thr<br>155 | Glu Met Arg Thr                                                                                                                                                                                                                                                                                                                                     | His<br>160             |
| Cys His Thr A                       | Asp Thr T<br>165  | nr Thr Ser                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Leu Pro His<br>170 | Phe His Val Ser<br>175                                                                                                                                                                                                                                                                                                                              | Ala,                   |
| Gly Gly Val G                       | Gly Pro T         | ar Thr Leu                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Gly Ser Asn        | Arg Glu Ile Thr                                                                                                                                                                                                                                                                                                                                     | Trp                    |

185 Thr Tyr Ser Glu Gly Lys Ile Phe Phe Tyr Phe Leu Gly Asn Gln Ala 195 200 205 Arg Leu Cys Leu Lys Lys Arg Lys Lys Gln Tyr Thr Val 215 . 220 <210> 480 <211> 144 <212> PRT <213> Homo sapiens <400> 480 Met Glu Pro Tyr Arg Gly Asn Glu Gln Pro Ser Gln Glu Gln Gly Val 10 Cys Cys Leu Trp Gly Leu Gln Ser Leu Pro Gln Gly Ser Tyr Val Thr Val Gly Phe Leu Val Val Lys Arg Gln Thr Ile Gly Arg Leu Glu Arg Asp Phe Met Phe Lys Cys Arg Lys Gln Pro Gly Leu Pro Pro Ser Gly Leu Cys Leu Leu Trp Pro Trp Pro Asn Leu Glu Phe Gly Arg Arg Gln Asp Arg Leu Thr Trp Ser Ser Val Ser Val Ala Gly Val Cys Ala Cys 85 Arg Ala Arg Pro Gly Trp Leu Gly Glu Gln Pro Ala Thr Ser Ala Gly 105 110 Val Arg Leu Glu Gln Val Glu Gln Pro Pro Ala His Pro Leu Gln Glu 115 120 125 Ala Gly Val Ala Arg Phe Pro Arg Pro Glu Trp Val Pro Pro Asn Gly **135** 140 <210> 481

Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys Ser His Ser 35 40 Leu Ser Gly Cys His Leu Met Ala Asp Gly Ala Lys Ala Leu Gly Lys Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr Asp Val Pro Cys Pro Ala Ala Ser Glu Val Gly Gly Cys Ala Pro Ser Ser Trp Arg 90 Ala Leu Ala Glu Val Thr Gly Cys Ser Leu Gly Pro Leu Gly Leu Ala Gln His Ala Gln Ala Ser Val Leu Leu Cys Tyr Lys Trp Ser His Ile Gly Glu Thr Ser Ser Ris Leu Arg Ser Lys Val Tyr Ala Ala Phe 135 Gly Gly Ser Ser Pro Cys Leu Lys Gly Leu Met Ser Leu Trp Ala Ser 150 155 Trp Leu Ser Arg Gly Arg Pro 165 <210> 482 <211> 143 We shall discuss that the state of  $\mathcal{S}_{ij}$  and  $\mathcal{S}_{ij}$ <212> PRT <213> Homo sapiens and the state of the state of the state of the state of <400> 482 Met Glu Pro Tyr Arg Gly Asn Lys Lys Gln Val Gln Glu Lys Gly Val Pro Cys Leu Trp Gly Ser Ser Pro Cys Leu Arg Cys His Met Ala Leu Arg Ala Ser Trp Leu Pro Gly Gly Gly Pro Gln Ala Ile Leu Gly Arg Thr Leu Cys Ser Ser Ala Glu Ser Ser Gln Asp Cys His Pro Gly Gly Pro Ser Ile Ala Leu Ala Lys Pro Cys Arg Gly Val Trp Leu Leu Phe Glu Pro Ala Trp Pro Pro Trp His Ala Arg Ala Pro Gly Ala Gly Three Leu Leu Arg Val Cys Leu Ser Cys Leu Gly Cys His Leu Cys Gly Gly 110

Ala Ser Gly Gly Gly Pro Ala Thr Asn Leu Thr Gln Ser Arg Lys

125

<400> 485

gggaagetta teacetatgt geegeetety e

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Cys Cys Leu Trp Gly Ser Ser Pro Cys Leu Gly Ser Tyr Gly Thr Ala
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Gly Phe Leu Val Ala Lys Arg Arg Thr Thr Gly Leu Leu Glu Glu Asp
Phe Thr Phe Lys Cys Arg Lys Gln Pro Lys Leu Pro Ser Met Arg Leu
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                                    60
Ser Leu Leu Trp Pro Trp Arg Asp Leu Lys Phe Val Pro Arg Gln Asp
Lys Leu Thr Arg Ser Ser Val Ser Val Ala Gly Ala Tyr Ala Cys Arg
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Thr Gly Phe Thr
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Leu Ala Ser Leu
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Tyr Thr Leu Ala Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro
1
                                  10
                                                    15
Lys Tyr Arg Gly
           20
     <210> 494
     <211> 20
     <212> PRT
     <213> Artificial Sequence
     <220>
     <223> Made in a lab
               <400> 494
Leu Pro Lys Tyr Arg Gly Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser 1 5 10 15
                                                    15
Leu Met Ile Ser
```

```
<210> 495
    <211> 20
    <212> PRT
    <213> Artificial Sequence
    <220>
    <223> Made in a lab
    <400> 495
Asp Ser Leu Met Thr Ser Phe Leu Pro Gly Pro Lys Pro Gly Ala Pro
Phe Pro Asn Gly
         20
    <210> 496
    <211> 21
    <212> PRT
    <213> Artificial Sequence
    <220>
    <223> Made in a lab
Ala Pro Phe Pro Asn Gly His Val Gly Ala Gly Gly Ser Gly Leu Leu
                                     82 Lat - 15 7 3 7 1
                         . 10
1
  . 5
Pro Pro Pro Pro Ala
         20
    <210> 497
    <211> 20
    <212> PRT
    <213> Artificial Sequence
    <220>
    <223> Made in a lab
Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser Ala Cys Asp Val
Ser Val Arg Val
                           97
         20
    <210> 498
    <211> 20
    <212> PRT
    <213> Artificial Sequence
    <220>
    <223> Made in a lab
    <400> 498
Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala Arg Val and val
Val Pro Gly Arg
         20
                                              42 315 W
```

```
<210> 499
     <211> 20
     <212> PRT
     <213> Artificial Sequence
     <223> Made in a lab
     <400> 499
Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp
              5 10
                                     15
Ser Ala Phe Leu
     20
     <211> 20
<212> PRT
<213> Artificial Sequence
     <223> Made in a lab
     <400> 500
Leu Asp Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met
                        10
Gly Ser Ile Val
     <210> 501
     <211> 20
     <212> PRT
     <213> Artificial Sequence
     <220>
     <223> Made in a lab
     <400> 501
Phe Met Gly Ser Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met
                                                  15
1
Val Ser Ala Ala
          20
     <210> 502
     <211> 414
     <212> DNA
     <213> Homo Sapien
     <220>
     <221> misc_feature
     <222> (1)...(414)
     <223> n=A,T,C or G
     <400> 502
caccatggag acaggeetge getggetttt cetggteget gtgetcaaag gtgtecaatg
tcagtcggtg gaggagtccg ggggtcgcct ggtcacgcct gggacacctt tgacantcac
                                                               120
ctgtagagtt tttggaatng acctcagtag caatgcaatg agctgggtcc gccaggctcc
                                                               180
agggaagggg ctggaatgga tcggagccat tgataattgt ccacantacg cgacctgggc
                                                               240
```

```
gaaaggccga ttnatnattt ccaaaacctn gaccacggtg gatttgaaaa tgaccagtcc
                                                                                300
 gacaaccgag gacacggcca cctatttttg tggcagaatg aatactggta atagtggttg
                                                                                360
gaagaatatt tggggcccag gcaccctggt caccgtntcc tcagggcaac ctaa
                                                                                 414
        <210> 503
        <211> 379
        <212> DNA
        <213> Homo Sapien
        <220>
        <221> misc_feature
        <222> (1)...(379)
        <223> n=A,T,C or G
       <400> 503
 atnogatggt gottggtcaa aggtgtccag tgtcagtcgg tggaggagtc cgggggtcgc
 ctggtcacgc ctgggacacc cctgacactc acctgcaccg tntctggatt ngacatcagt
 agctatggag tgagctgggt ccgccaggct ccagggaagg ggctggnata catcggatca 180
 ttagtagtag tggtacattt tacgcgagct gggcgaaagg ccgattcacc atttccaaaa cctngaccac ggtggatttg aaaatcacca gtttgacaac cgaggacacg gccacctatt
 tntgtgccag aggggggttt aattataaag acatttgggg cccaggcacc ctggtcaccg
 tntccttagg gcaacctaa
        <210> 504
        <211> 19 (16.2) (16.1) (20.1) (2)
                                         (s i
        <212> PRT - (
        <213> Artificial Sequence
        <220>
        <223> Made in a lab
                                                                    War Library
                                                                    35 K 135
        <400> 504
 Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp Ser Pro Tyr Phe Lys Glu
 1
                                                                15
 Asn Ser Ala
        <210> 505
        <211> 20
        <212> PRT
        <213> Artificial Sequence
        <220>
        <223> Made in a lab
       <400> 505
 Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn Asp Asn Val Thr
 1
                                         10
                                                                15
 Asn Thr Ala Asn
                                                          បានបាននៅក្នុងទៀត ស ប្រុ
              20
                                                           and the second
                                                         Down 1,7 rm 32.5
       <210> 506
       <211> 407
       <212> DNA 1 48 (State & Local Republication of Configuration agree) provide as
       <213> Homo Sapien (District Problems) - Browning Browning grap problems and per superior
                  ်လိုလ်ပြီး ကရာလူနောက်လျှင် (ရာသည် နှစ်ရှိတွေနေ) မှုနှစ်ပြုနှစ်ပြုနှစ်ပြုနှစ်ပြုနှစ်များကြောင့် များများများများ
                      ்ற நின்னை நடித்த நட
```

```
atggagacag gcctgcgctg gcttctcctg gtcgctgcgc tcaaaggtgt ccagtgtcag
                                                                        60
tcgctggagg agtccggggg tcgcctggtc acgcctggga cacccctgac actcacctgc
                                                                       120
acceptctctg gattctccct cagtagcaat gcaatgatct gggtccgcca ggctccaggg
                                                                       180
aaggggctgg aatacatcgg atacattagt tatggtggta gcgcatacta cgcgagctgg
                                                                       240
                                                                       300
gtgaaaggcc gattcaccat, ctccaaaacc tcgaccacgg tggatctgag aatgaccagt
                                                                       360
ctgacaaccg aggacacggc cacctatttc tgtgccagaa atagtgattt tagtggtatg
                                                                       407
ttgtggggcc caggcaccct ggtcaccgtc tcctcagggc aacctaa
      <210> 507
      <211> 422
      <212> DNA
      <213> Homo Sapien
      <400> 507
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                                                                        60
teggtggagg agteeggggg tegeetggte acgeetggga cacceetgae acteacetgt
                                                                       120
acagtetete gatteteet cagcaactae gacetgaact gggteegeea ggeteeaggg
                                                                       180
aaggggctgg aatggatcgg gatcattaat tatgttggta ggacggacta cgcgaactgg
                                                                       240
gcaaaaggcc ggttcaccat ctccaaaacc tcgaccaccg tggatctcaa gatcgccagt
                                                                       300
ccgacaaccg aggacacggc cacctatttc tgtgccagag ggtggaagtg cgatgagtct
                                                                       360
ggtccgtgct tgcgcatctg gggcccaggc accetggtca ccgtctcctt agggcaacct
                                                                       420
                                                                       422
aa
      <210> 508
      <211> 411
      <212> DNA
      <213> Homo Sapien
      <220>
      <221> misc feature
      <222> (1) ... (411)
      <223> n=A,T,C or G
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cggtggagga gtccgggggt cgcctggtca cgcctgggac acccctgaca ctcacctgca
                                                                        120
                                                                        180
carteteteq aatequeete agtagetact geatgagetg ggteegeeag geteeaggga
                                                                        240
aggggctgga atggatcgga atcattggta ctcctggtga cacatactac gcgaggtggg
cgaaaggccg attcaccatc tccaaaacct cgaccacggt gcatntgaaa atcnccagtc
                                                                        300
cgacaaccga ggacacggcc acctatttct gtgccagaga tcttcgggat ggtagtagta
                                                                        360
                                                                        411
ctggttatta taaaatctgg ggcccaggca ccctggtcac cgtctccttg g
      <210> 509
       <211> 15
       <212> PRT
       <213> Artificial Sequence
       <220>
       <223> Made in a lab
       <400> 509
Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
                                    10
       <210> 510
       <211> 15
       <212> PRT
       <213> Artificial Sequence
```

```
<220>
                        <223> Made in a lab 🧪
                        Pro Glu Tyr Asn Arg Pro Leu Leu Ala Asn Asp Leu Met Leu Ile
                                                               <210> 511
                         <211> 15
                         <212> PRT
                         <213> Artificial Sequence
                        <220>
                     ►<223> Made (in a lab Asset ) He to the end of the transfer of the transfer
                         The same of the second seconds of the second seconds of the second seconds of the second seconds.
                         <400> 511 cgg / n ny mag mg is leg | and a mag mag mag is leg | less g is a
                           ်ပြုပြုပြုသည့် များများ ကျခာရှိမှုတစ်စွာမှု နေသူများကြောင်းပါတယ်သည်။ များများများကြောင်းမြေးသည်။ များများများမ
Tyr His Pro Ser Met Phe Cys Ala Gly Gly Gln Asp Gln Lys
                        <210> 512
                         <211> 15
                                                                                                                                                                                                                                             in Community of the State of th
                         <212> PRT
                         <213> Artificial Sequence
                                                                                                                                                                                                                                             8181 a.C
                         <220>
                        <223> Made in a lab
                                                                                                                                                                                                         California de la Color
                         <400> 512
Asp Ser Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu

1 5 10 15
                        <210> 513
                       1.54
                        . 4
                        <400> 513
Ala Pro Cys Gly Gln Val Gly Val Pro Asx Val Tyr Thr Asn Leu
                                                                                                                                                                             15
                                                                    5 10
    1
                        <210> 514
                        <211> 15
                         <212> PRT
                                                                                                                                                                                                                   12 %.
                         <213> Artificial Sequence
                        <220>
                         <223> Made in allabase of the style of the s
                        <400> 514
Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
                                                                                                                                                                                                                                      15
                                                                                                                                                   10
    1
                                                                                                                                                                                 3
                        <210> 515
```

```
<211> 15
      <212> PRT
      <213> Artificial Sequence
      <220>
      <223> Made in a lab
      <400> 515
Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg
, 1
      5 . .
                                   10
      <210> 516
      <211> 15
      <212> PRT
      <213> Artificial Sequence
      <220>
      <223> Made in a lab
      <400> 516
Val Ser Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln
      <210> 517
      <211> 15
      <212> PRT
      <213> Artificial Sequence
      <220>
      <223> Made in a lab
      <400> 517
Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met
                                                       15
      <210> 518
      <211> 15
      <212> PRT
      <213> Artificial Sequence
      <220>
      <223> Made in a lab
      <400> 518
Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly
 1
                                   10
                                                          NEW STATE
      <210> 519
      <211> 17
      <212> PRT
      <213> Artificial Sequence
      <220>
      <223> Made in a lab
      <400> 519
Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg Asn Tyr Asp Glu Gly Cys
                                   10
```

```
Gly
      <210> 520
      <211> 25
      <212> PRT
      <213> Artificial Sequence
      <223> Made in a lab
      <400> 520
Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly Thr
                      10
Glu Ala Arg Arg His Tyr Asp Glu Gly
      <210> 521
      <211> 21
      <213> Artificial Sequence 3 and a 3
      <223> Made in a lab
      <400> 521
Ala Pro Phe Pro Asn Gly His Val Gly Ala Gly Gly Ser Gly Leu Leu
               5
1
Pro Pro Pro Pro Ala
           20
      <210> 522
      <211> 20
      <212> PRT
      <213> Artificial Sequence
      <220>
      <223> Made in a lab
      <400> 522
Leu Leu Val Val Pro Ala Ile Lys Lys Asp Tyr Gly Ser Gln Glu Asp
1
                                   10
Phe Thr Gln Val
           20
     <210> 523
     <211> 254
      <212> PRT
     <213> Artificial Sequence
     <220>
     <223> Made in a lab
     <220>
     <221> VARIANT
     <222> (1)...(254)
     <223> Xaa = any amino acid
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```
<400> 523
 Met Ala Thr Ala Gly Asn Pro Trp Gly Trp Phe Leu Gly Tyr Leu Ile
                                        10
Leu Gly Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile
                                   25
 Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu
                               40
 Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val Ris Pro Gln
                          55
 Trp Val Leu Ser Ala Thr His Cys Phe Gln Asn Ser Tyr Thr Ile Gly
                      70
 Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met
                                        90
 Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu
                                   105
 Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu
                               120
                                                  125
 Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala
                         135
 Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg
                      150
                                           155
 Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu
                                       170
 Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys
                               185
 Ala Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser Gly
                   200
                                                    205
 Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly
                                                220
              Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu
                  230 235
 Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
                  245 250
<210> 524
<211> 765
<212> DNA
<213> Homo sapien
<400> 524
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ggategeteg tetetggtag etgeageeaa ateataaaeg gegaggaetg eageeegeae
                                                                           120
togcagocot ggcaggoggc actggtcatg gaaaacgaat tgttctgctc gggcgtcctg
                                                                           180
gtgcatccgc agtgggtgct gtcagccgca cactgtttcc agaactccta caccatcggg 240 ctgggcctgc acagtcttga ggccgaccaa gagccaggga gccagatggt ggaggccagc 300
ctgggcctgc acagtcttga ggccgaccaa gagccaggga gccagatggt ggaggccagc 300 ctctccgtac ggcacccaga gtacaacaga cccttgctcg ctaacgacct catgctcatc 360
aagttggacg aatccgtgtc cgagtctgac accatccgga gcatcagcat tgcttcgcag 420
atgectaceg tgetgeagtg egtgaacgtg teggtggtgt etgaggaggt etgeagtaag 540 etetatgace egetgtacea eeccageatg ttetgaggaggt etgeagtaag 540
gactectgea acggtgacte tggggggece etgatetgea acgggtactt geagggeett
                                                                          720
gtgtctttcg gaaaagcccc gtgtggccaa gttggcgtgc caggtgtcta caccaacctc
tgcaaattca ctgagtggat agagaaaacc gtccaggcca gttaa
<210> 525 ·
                       त्रा दिश्वक स्थान । १००० हिन्दु स्थानी के जन्म है । १००० है
<212> PRT
<211> 254
<213> Homo sapien
```

<400> 525

```
Met Ala Thr Ala Gly Asn Pro Trp Gly Trp Phe Leu Gly Tyr Leu Ile
                                    10
Leu Gly Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile
                                25
                                                    30
Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu
                            40
Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln
                                        60
                        55
Trp Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly
                                     75
Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met
                                    90
                                                        95
Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu
                                       17.1
                                                   110
                              · 105
Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu
                            120
                                                125
Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala
                        135
                                            140
Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg
                    150
                                        155
                                                            160
Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu
                                    170
                                                        175
                165
                                                    7. 3
Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys
            180
                                                    190
                                185
Ala Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly
                            200
                                                205
Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly
                        215
                                            220
Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu
                                       235
                    230
                                                            240
Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
                245
                                    250
<210> 526
<211> 963
<212> DNA
<213> Homo sapiens
                      3.5
atgagttcct gcaacttcac acatgccacc tttgtgctta ttggtatccc aggattagag 60
aaagcccatt totgggttgg ottocccotc otttocatgt atgtagtggc aatgtttgga 120
aactgcatcg tggtcttcat cgtaaggacg gaacgcagcc tgcacgctcc gatgtacctc 180
tttetetgea tgettgeage cattgacetg geettateea catecaccat geetaagate 240
cttgcccttt tctggtttga ttcccgagag attagctttg aggcctgtct tacccagatg 300
ttetttatte atgecetete agecattgaa tecaccatee tgetggecat ggeetttgae 360
cgttatgtgg ccatctgcca cccactgcgc catgetgcag tgctcaacaa tacagtaaca 420
goodagattg goatogtggc tgtggtoogo ggatocotot tttttttocc actgcctctg 480
ctgatcaage ggctggcctt ctgccactcc aatgtcctct cgcactccta ttgtgtccac 540
caggatgtaa tgaagttggc ctatgcagac actitgccca atgtggtata tggtcttact 600
gccattctgc tggtcatggg cgtggacgta atgttcatct ccttqtccta ttttctqata 660
atacgaacgg ttctgcaact gccttccaag tcagagcggg ccaaggcctt tggaacctgt 720
gtgtcacaca ttggtgtggt actcgccttc tatgtgccac ttattggcct ctcagttgta 780
caccgctttg gaaacagcct tcatcccatt gtgcgtgttg tcatgggtga catctacctg 840
ctgctgcctc ctgtcatcaa tcccatcatc tatggtgcca aaaccaaaca gatcagaaca 900
cgggtgctgg ctatgttcaa gatcagctgt gacaaggact tgcaggctgt gggaggcaag 960
tga
                                                           િકેટ ેંં ક63ે ડે
```

| <210   | )> 52 | 27     |       |          |        |            |      |              |          |          |            |                |                   |              |                   |                                        |          |
|--------|-------|--------|-------|----------|--------|------------|------|--------------|----------|----------|------------|----------------|-------------------|--------------|-------------------|----------------------------------------|----------|
| <211   | L> 32 | 0      |       | 1        |        | 1          |      |              |          |          |            |                |                   |              |                   | _                                      |          |
| <212   | 2> PF | T      | 1.1   | -        | 1      |            |      |              |          |          |            | •              |                   | •            |                   |                                        | ** *     |
| <213   | 3> Hc | mo s   | sapie | ens      | 11     |            |      |              |          |          |            |                |                   |              |                   |                                        |          |
|        |       |        | _     |          | 1      |            |      |              |          |          |            |                |                   |              |                   |                                        |          |
| <400   | )> 52 | 27     |       |          |        | · · ·      |      |              |          |          |            |                |                   |              |                   | 2.12                                   |          |
| Met    | Ser   | Ser    | Cvs   | Asn      | Phe    | Thr        | His  | Ala          | Thr      | Phe      | Val        | Leu            | Ile               | Gly          | Ile               | •                                      |          |
|        |       |        | -2-   | 5        |        |            | 4    |              | 10       |          |            |                |                   | 15           |                   |                                        |          |
|        |       |        |       |          |        |            |      |              |          |          |            |                |                   |              |                   |                                        |          |
| D      | Gly   | T      | C3    | T        | אוה    | uic        | Pho  | Trans        | 7727     | G1 17    | Phe        | Pro            | T.011             | T.e11        | Ser               |                                        |          |
| Pro    | GTĀ   | теп    |       | тЛя      | ALG    | птэ        | FIIE |              | Val      | GTA      | File       | 1.10           | 30                |              | -                 |                                        |          |
|        |       |        | 20    |          |        |            |      | 25           |          | ***      |            |                | 30                |              |                   |                                        |          |
|        |       | _      | _     |          | 1.     |            | 1    | _            | _        |          | 7          | ** - 7         | DI                | <b>-</b> 1 - | 77-7              |                                        |          |
| Met    | Tyr.  | -Val   | Val   | Ala      | Met    | Phe        |      | Asn          | Cys      | тте      | vaı        |                | Pne               | тте          | var               |                                        |          |
|        |       | 35     | ,     | ' ;      | 1-     |            | 40   |              |          |          |            | 45             |                   |              |                   |                                        |          |
| ٠.     |       |        |       |          | 1      |            |      |              |          |          |            |                | -                 | •            |                   | : ' '                                  |          |
| Arg    | Thr   | Glu    | Arg   | Ser      | Leu    | His        | Ala  | Pro          | Met      | Tyr      | Leu        | Phe            | Leu               | Cys          | Met               |                                        |          |
| _      | 50    |        | _     |          |        | 55         |      |              |          |          | 60         |                |                   |              |                   | •                                      |          |
|        |       |        |       |          |        |            |      |              |          |          |            |                |                   |              |                   |                                        |          |
| T.e.11 | Ala   | Ala    | Tle   | Asp      | Leu    | Ala        | Leu  | Ser          | Thr      | Ser      | Thr        | Met            | Pro               | Lys          | Ile               | •                                      |          |
| 65     |       |        |       |          | 70     | -,         |      |              |          | 75       | 1          |                |                   | , <b>-</b>   | 80                |                                        | t        |
| 05     |       |        | ľ     | •        |        |            |      | •            |          |          |            |                |                   |              |                   |                                        | ,        |
| T      | Ala   | T      | Db.   | (T)      | Dho    | 7.00       | 202  | 70.00        | Glu      | Tle      | Sar        | Phe            | Glu               | Δla          | Cvs               |                                        |          |
| ren    | ALA   | ren    | Pne   |          |        | Asp        | SeT  | ALG          |          | 110      | Det        | LIIC           | 01.4              | 95           | 03.5              |                                        |          |
|        |       |        |       | 85       | ı      |            |      |              | 90       |          |            |                |                   | - 33         |                   |                                        |          |
|        |       |        |       |          |        |            | •    |              | <b>-</b> | <b>~</b> | 77.        | <b>-</b> 1-    | 03                | G            | (II)              |                                        |          |
| Leu    | Thr   | Gln    | Met   | Phe      | Phe    | Ile        | His  |              | Leu      | ser      | АТа        | тте            |                   | Ser          | Thr               |                                        | -        |
|        |       |        | 100   |          |        |            |      | 105          |          |          |            |                | 110               |              |                   |                                        |          |
|        |       |        |       |          |        |            |      |              |          |          |            |                |                   |              |                   | •                                      |          |
| Ile    | Leu   | Leu    | Ala   | Met      | Ala    | Phe        | Asp  | Arg          | Tyr      | Val      | Ala        | Ile            | Cys               | His          | Pro               |                                        | ·        |
|        |       | 115    |       |          |        |            | 120  |              |          |          |            | 125            |                   |              |                   |                                        |          |
|        |       |        |       |          |        |            |      |              |          |          |            |                |                   |              |                   | •                                      | :        |
| T.e.   | Arg   | His    | Ala   | Ala      | Val    | Leu        | Asn  | Asn          | Thr      | Val      | Thr        | Ala            | Gln               | Ile          | Gly               | •                                      | ٠.       |
|        | 130   |        |       |          |        | 135        |      |              |          |          | 140        |                | د. ا              |              |                   |                                        |          |
|        | -50   | ٠.     | . "   | :        | i -    |            |      |              | i        |          |            |                |                   |              | : 1               | •                                      |          |
| T1.    | 17-1  | ~ F /C | 37-1  | 1751     | 71 ~~~ | Ġlw        | Ser  | T.e.i        | Phe      | Phe      | Phe        | Pro            | Leu               | Pro          | Leu               |                                        |          |
|        | Val   | ALG    | AGT   | Val      | 150    | Q-3        |      |              |          | 155      |            | 1.5            |                   |              | 160               | 1                                      |          |
| 145    |       | , `    |       |          | 130    |            |      | , r          |          |          |            |                |                   |              |                   |                                        |          |
| _      |       |        | -     |          | ~ 1 -  | <b>5</b> 1 | 0    | T7.2         |          | ·A ca    | 1701       | T 011          | 802               | u4e          | Ser               |                                        |          |
| Leu    | тте   | гãs    | Arg   |          |        | Pne        | Cys  | HIS          |          |          | var        | ьец            | Ser               | 175          | Ser               |                                        |          |
|        |       |        | • •   | 165      |        |            |      | •            | 170      |          |            |                |                   | 175          |                   |                                        |          |
|        |       |        |       |          |        | •          |      |              |          | ·        | _          | ′ _ <b>-</b> ` |                   |              | · • · · ·         |                                        |          |
| Tyr    | Cys   | Val    | His   | Gln      | Asp    | Val        | Met  | Lys          | Leu      | Ala      | Tyr        | Ala            |                   | Thr          | Leu               | • . •                                  |          |
|        |       |        | 180   | i.,      |        |            |      | 185          | S . "    |          |            |                | 190               |              | • • • •           |                                        | 115      |
|        |       |        | 5     |          |        | •: •       |      | ٠.           | , š.     |          |            | Sec. 31        |                   | ' '          |                   | 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1  | 11 41 -1 |
| Pro    | Asn   | Val    | Val   | Tvr      | Gly    | Leu        | Thr  | `Ala         | Ile      | Leu      | Leu        | ·'Val          | Met               | Gly          | <b>Val</b>        |                                        | 1        |
|        |       | 195    |       |          | 1      |            | 200  |              |          |          |            | 205            | ) T :             | . ' !        | , * * * . <b></b> |                                        | aan t    |
|        |       |        |       | -        |        |            |      |              | • •      | 7 1      | 100        |                |                   |              | 1                 | s in the n                             | in the G |
| 7 ~~   | 17-1  | Mot    | Dho   | TIO      | 20*    | Lou        | Cor  | . Trir       | Phe      | Ten      | Tie        | Tle            | Ara               | Thr          | Val               | , ;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;;; | 5.5 × .  |
| Asp    |       | Met    | LITE  | TTE      | Ser    | 215        | Der  | - <b>y</b> - | , - 110  |          | 220        |                | 9                 |              |                   | 1000                                   |          |
|        | 210   | ٠,     |       |          |        | 213        |      |              | -        | er en er | 220        | .,             |                   |              |                   | 1.1                                    |          |
|        |       |        |       |          |        |            |      |              |          |          |            |                |                   |              |                   |                                        |          |
|        |       | Leu    | Pro   | Ser      | ьуs    | Ser        | GLU  | Arg          | ATa      | гys      | нта        | rne            | атХ               | ınr          | Cys               | 435<br>V 200                           |          |
| 225    |       |        | 1 8 2 |          | 230    |            |      | -            |          | 235      |            |                | - '               | 1.1          | <b>24</b> 0       | · Jane                                 |          |
|        |       |        |       | ₹ 3      | •      | ٠,         | . 4  |              | * 1.5 *  | riti i   |            |                | ': <sup>1</sup> · | 3 3 3 .<br>  |                   | a de                                   |          |
| Val    | Ser   | His    | Ile   | Gly      | Val    | Val        | Leu  | Ala          | · Phe    | Tyr      | Val        | Pro            | Leu               | Ile          | Gly               |                                        |          |
|        | ٠,    |        |       | 245      | . :    |            |      | ٠.           | 250      |          |            |                | , ,               | :255         | i e e             | 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1  | 1.       |
|        | .,    | .* `   | :     | -11, 15, | 1.4    |            |      | i. :         | ٠        |          | ; <b>*</b> | . *:           | 3. j              |              | 7                 | 4. 1                                   | H.25.    |
| Len    |       |        |       |          | e 🕳 😅  | <b>53</b>  | 07:  | 71           | C        | · T      | 27412      | Dwa            | Tia               | 37-7         | 71                |                                        |          |
| u      |       |        | . 250 |          | 9      |            | 2    | 265          | 1.00     |          |            |                | 270               |              | Arg               | 4.4.2                                  |          |
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Ile Ile Tyr Gly Ala Lys Thr Lys Gln Ile Arg Thr Arg Val Leu Ala
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Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val Val Ala Trp Gly Asp
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    50 55
Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr His Val His Gly Glu
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Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Arg Asp
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                             105
Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser
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                                            125
Glu Val Val Lys L u Val Leu Asp Arg Cys Gln Leu Asn Val Leu
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Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu 225 230 245 255  Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu Glu Gln Asn Val Asp 260 270  Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu Ser Met Leu Phe Leu 275 280  Val Ile Ile Met 290 <a href="#"> &lt;</a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a> | ·                                                                                                                                                                                                                                                                                                         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| Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Val Tyr Asn Glu 190  Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu 205  Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Gly Ile His Glu 210  Cln Lys Gln Gln Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu 225 230  Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys 245  Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu Glu Gln Asn Val Asp 265  Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu Ser Met Leu Phe Leu 275  Val Ile Ile Met 290                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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 |                                                                  | Met                                                                                    | Leu                                                                         | Leu G                                                                        |                                                                                                   |                                                                                      | Thr                                                                                  | Asp                                                                                 | Pro                                                                                                                                                                                                                                                                                                                                  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| Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Cly Ile His Glu 210  215  Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Cly Ile His Glu 220  Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu 225  230  230  235  Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys 245  Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu Glu Gln Asn Val Asp 260  265  Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu Glu Gln Asn Val Asp 275  Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu Ser Met Leu Phe Leu 275  Val Ile Ile Met 290                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                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| Gin Lys Gin Gin Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu 225 230 235 240  Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys 245 250 255  Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu Glu Gln Asn Val Asp 260 265 270  Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu Ser Met Leu Phe Leu 275 280 285  Val Ile Ile Met 290 <a href="mailto:club Arg Arg Pro Glu Ser Met Leu Phe Leu 275">Club Phe Leu 275</a> Val Ile Ile Met 290 <a href="mailto:club Arg Arg Pro Glu Ser Met Leu Phe Leu 275">Club Phe Leu 275</a> Val Ile Ile Met 290 <a href="mailto:club Arg Arg Pro Glu Ser Met Leu Phe Leu 285">Club Phe Leu 285</a> Val Ile Ile Met 290 <a href="mailto:club Arg Arg Pro Glu Ser Met Leu Phe Leu 295">Club Phe Leu 285</a> Val Ile Ile Met 290 <a href="mailto:club Arg Arg Pro Glu Ser Met Leu Phe Leu 285">Club Phe Leu 285</a> Val Ile Ile Met 290 <a href="mailto:club Arg Arg Pro Glu Ser Met Leu Phe Leu 285">Club Phe Leu 285</a> Val Ile Ile Met 290 <a 285"="" arg="" glu="" href="mailto:club Arg Arg Pro Glu Ser Met Leu Phe Leu 285&lt;/a&gt;  Val Ile Ile Met 290  &lt;a href=" leu="" mailto:club="" met="" phe="" pro="" ser="">Club Phe Leu 285</a> Val Ile Ile Met 290 <a 285<="" a="" arg="" glu="" href="mailto:club Arg Arg Pro Glu Ser Met Leu Phe Leu 285&lt;/a&gt;  Val Ile Ile Met 290  &lt;a href=" leu="" mailto:club="" met="" phe="" pro="" ser="">  Val Ile Ile Met 290  <a 285<="" a="" arg="" glu="" href="mailto:club Arg Arg Pro Glu Ser Met Leu Phe Leu 285&lt;/a&gt;  Val Ile Ile Met 290  &lt;a href=" leu="" mailto:club="" met="" phe="" pro="" ser="">  Val Ile Ile Met 290  <a 285<="" a="" arg="" glu="" href="mailto:club Arg Arg Pro Glu Ser Met Leu Phe Leu 285&lt;/a&gt;  Val Ile Ile Met 290  &lt;a href=" leu="" mailto:club="" met="" phe="" pro="" ser="">  Val Ile Ile Met 290  <a 285<="" a="" arg="" glu="" href="mailto:club Arg Arg Pro Glu Ser Met Leu Phe Leu 285&lt;/a&gt;  Val Ile Ile Met 290  &lt;a href=" leu="" mailto:club="" met="" phe="" pro="" ser="">  215   Val Ile Ile Met 290  <a 285<="" a="" arg="" glu="" href="mailto:club Arg Arg Pro Glu Ser Met Leu Phe Leu 285&lt;/a&gt;  2265  Val Ile Ile Met 290  &lt;a href=" leu="" mailto:club="" met="" phe="" pro="" ser="">  2265  Val Ile Ile Met 290</a></a></a></a></a>                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 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| Val Ile Ile Met 290 <pre> &lt;210&gt; 533 &lt;211&gt; 801 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  </pre> <pre> &lt;400&gt; 533 atgtacaagc ttcagtgcaa caactgtgct acaaatggag ccacagagag gaaacaagca 60 gcaggctcag gagcagggta tgcgctgct tcggctctcc aatccatgcc tcagggctcc 120 tatgccactg cacgattctt ggttgccaag aggccaacca caggccatct tgagaaggag 180 tttatgttcc actgcagaaa gcagcagga tcaccatca ggggacttgg tcttctgtgg 240 ccctggccag acatagaatt tgtgccaagg caggacaagc tcactcagag caggctgtta 300 gtacctcaaa tctgtgcgtg ccagacaagg ccaaactggc tcaatgagca accagccacc tctgcagggg tgcgtctgga ggaggtggac cagccaccaa ccttacccag tcaaggaagt 420 ggatggccat gttcccacag cctgagtggc tgccacctga tggctgatat agcaaaggcc 480</pre>                                                                                                                                                                                                                                                                                                                         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| <pre>&lt;211&gt; 801 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;400&gt; 533 atgtacaage ttcagtgcaa caactgtgct acaaatggag ccacagagag gaaacaagca 60 gcaggctcag gagcagggta tgcgctgcct tcggctctcc aatccatgce tcagggctcc 120 tatgccactg cacgattctt ggttgccaag aggccaacca caggccatct tgagaaggag 180 tttatgttcc actgcagaaa gcagccagga tcaccatcca ggggacttgg tcttctgtgg 240 ccctggccag acatagaatt tgtgccaagg caggacaagc tcactcagag cagcgtgtta 300 gtacctcaaa tctgtgcgtg ccagacaagg ccaaactggc tcaatgagca accagccacc 360 tctgcagggg tgcgtctgga ggaggtggac cagcaccaa ccttacccag tcaaggaagt 420 ggatggccat gttcccacag cctgagtggc tgccacctga tggctgatat agcaaaggcc 480</pre>                                                                                                                                                                                                                                                                                                                                                                     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| <pre>&lt;211&gt; 801 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;400&gt; 533 atgtacaage ttcagtgcaa caactgtgct acaaatggag ccacagagag gaaacaagca 60 gcaggctcag gagcagggta tgcgctgcct tcggctctcc aatccatgce tcagggctcc 120 tatgccactg cacgattctt ggttgccaag aggccaacca caggccatct tgagaaggag 180 tttatgttcc actgcagaaa gcagccagga tcaccatcca ggggacttgg tcttctgtgg 240 ccctggccag acatagaatt tgtgccaagg caggacaagc tcactcagag cagcgtgtta 300 gtacctcaaa tctgtgcgtg ccagacaagg ccaaactggc tcaatgagca accagccacc 360 tctgcagggg tgcgtctgga ggaggtggac cagcaccaa ccttacccag tcaaggaagt 420 ggatggccat gttcccacag cctgagtggc tgccacctga tggctgatat agcaaaggcc 480</pre>                                                                                                                                                                                                                                                                                                                                                                     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| <pre>&lt;211&gt; 801 &lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;400&gt; 533 atgtacaage ttcagtgcaa caactgtgct acaaatggag ccacagagag gaaacaagca 60 gcaggctcag gagcagggta tgcgctgcct tcggctctcc aatccatgce tcagggctcc 120 tatgccactg cacgattctt ggttgccaag aggccaacca caggccatct tgagaaggag 180 tttatgttcc actgcagaaa gcagccagga tcaccatcca ggggacttgg tcttctgtgg 240 ccctggccag acatagaatt tgtgccaagg caggacaagc tcactcagag cagcgtgtta 300 gtacctcaaa tctgtgcgtg ccagacaagg ccaaactggc tcaatgagca accagccacc 360 tctgcagggg tgcgtctgga ggaggtggac cagcaccaa ccttacccag tcaaggaagt 420 ggatggccat gttcccacag cctgagtggc tgccacctga tggctgatat agcaaaggcc 480</pre>                                                                                                                                                                                                                                                                                                                                                                     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| <pre>&lt;212&gt; DNA &lt;213&gt; Homo sapiens  &lt;400&gt; 533 atgtacaage ttcagtgcaa caactgtgct acaaatggag ccacagagag gaaacaagca 60 gcaggctcag gagcagggta tgcgctgcct tcggctctcc aatccatgcc tcagggctcc 120 tatgccactg cacgattctt ggttgccaag aggccaacca caggccatct tgagaaggag 180 tttatgttcc actgcagaaa gcagccagga tcaccatcca ggggacttgg tcttctgtgg 240 ccctggccag acatagaatt tgtgccaagg caggacaagc tcactcagag cagcgtgtta 300 gtacctcaaa tctgtgcgtg ccagacaagg ccaaactggc tcaatgagca accagccacc 360 tctgcagggg tgcgtctgga ggaggtggac cagccaccaa ccttacccag tcaaggaagt 420 ggatggccat gttcccacag cctgagtggc tgccacctga tggctgatat agcaaaggcc 480</pre>                                                                                                                                                                                                                                                                                                                                                                                    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| <213> Homo sapiens <400> 533 atgtacaagc ttcagtgcaa caactgtgct acaaatggag ccacagagag gaaacaagca 60 gcaggctcag gagcagggta tgcgctgcct tcggctctcc aatccatgcc tcagggctcc 120 tatgccactg cacgattctt ggttgccaag aggccaacca caggccatct tgagaaggag 180 tttatgttcc actgcagaaa gcagccagga tcaccatcca ggggacttgg tcttctgtgg 240 ccctggccag acatagaatt tgtgccaagg caggacaagc tcactcagag cagcgtgtta 300 gtacctcaaa tctgtgcgtg ccagacaagg ccaaactggc tcaatgagca accagccacc 360 tctgcagggg tgcgtctgga ggaggtggac cagccaccaa ccttacccag tcaaggaagt 420 ggatggccat gttcccacag cctgagtggc tgccacctga tggctgatat agcaaaggcc 480                                                                                                                                                                                                                                                                                                                                                                                                                            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| <400> 533 atgtacaagc ttcagtgcaa caactgtgct acaaatggag ccacagagag gaaacaagca 60 gcaggctcag gagcagggta tgcgctgcct tcggctctcc aatccatgcc tcagggctcc 120 tatgccactg cacgattctt ggttgccaag aggccaacca caggccatct tgagaaggag 180 tttatgttcc actgcagaaa gcagccagga tcaccatcca ggggacttgg tcttctgtgg 240 cctggccag acatagaatt tgtgccaagg caggacaagc tcactcagag cagcgtgtta 300 gtacctcaaa tctgtgcgtg ccagacaagg ccaaactggc tcaatgagca accagccacc 360 tctgcagggg tgcgtctgga ggaggtggac cagcaccaa ccttacccag tcaaggaagt 420 ggatggccat gttcccacag cctgagtggc tgccacctga tggctgatat agcaaaggcc 480                                                                                                                                                                                                                                                                                                                                                                                                                                                 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| atgtacaage ttcagtgcaa caactgtgct acaaatggag ccacagagag gaaacaagca 60 gcaggetcag gagcagggta tgcgctgcet teggetetec aatccatgee teagggetee 120 tatgccactg cacgattett ggttgccaag aggccaacca caggccatet tgagaaggag 180 tttatgttce actgcagaaa gcagccagga tcaccateca ggggacttgg tettetgtgg 240 ccetggccag acatagaatt tgtgccaagg caggacaage tcactcagag cagegtgtta 300 gtacetcaaa tetgtgcgtg ccagacaagg ccaaactgge tcaatgagca accagccacc 360 tctgcagggg tgcgtctgga ggaggtggac cagccaccaa ccttacccag tcaaggaagt 420 ggatggccat gttcccacag cctgagtgge tgccacctga tggctgatat agcaaaggce 480                                                                                                                                                                                                                                                                                                                                                                                                                                                         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| gcaggctcag gagcagggta tgcgctgcct tcggctctcc aatccatgcc tcagggctcc 120 tatgccactg cacgattctt ggttgccaag aggccaacca caggccatct tgagaaggag 180 tttatgttcc actgcagaaa gcagccagga tcaccatcca ggggacttgg tcttctgtgg 240 ccctggccag acatagaatt tgtgccaagg caggacaagc tcactcagag cagcgtgtta 300 gtacctcaaa tctgtgcgtg ccagacaagg ccaaactggc tcaatgagca accagccacc 360 tctgcagggg tgcgtctgga ggaggtggac cagccaccaa ccttacccag tcaaggaagt 420 ggatggccat gttcccacag cctgagtggc tgccacctga tggctgatat agcaaaggcc 480                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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| tatgccactg cacgattett ggttgccaag aggccaacca caggccatct tgagaaggag 180 tttatgttcc actgcagaaa gcagccagga tcaccatcca ggggacttgg tcttctgtgg 240 ccctggccag acatagaatt tgtgccaagg caggacaagc tcactcagag cagcgtgtta 300 gtacctcaaa tctgtgcgtg ccagacaagg ccaaactggc tcaatgagca accagccacc 360 tctgcagggg tgcgtctgga ggaggtggac cagcgaccaa ccttacccag tcaaggaagt 420 ggatggccat gttcccacag cctgagtggc tgccacctga tggctgatat agcaaaggcc 480                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    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| ccctggccag acatagaatt tgtgccaagg caggacaagc tcactcagag cagcgtgtta 300 gtacctcaaa tctgtgcgtg ccagacaagg ccaaactggc tcaatgagca accagccacc 360 tctgcagggg tgcgtctgga ggaggtggac cagcgaccaa ccttacccag tcaaggaagt 420 ggatggccat gttcccacag cctgagtggc tgccacctga tggctgatat agcaaaggcc 480                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                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| gtaceteaaa tetgtgegtg ecagaeaagg eeaaactgge teaatgagea accageeace 360 tetgeagggg tgegtetgga ggaggtggae eageeaceaa eettaceeag teaaggaagt 420 ggatggeeat gtteecacag eetgagtgge tgeeacetga tggetgatat ageaaaggee 480                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      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| tetgeagggg tgegtetgga ggaggtggae eagegaeeaa eettaeeeag teaaggaagt 420<br>ggatggeeat gtteeeacag eetgagtgge tgeeaeetga tggetgatat ageaaaggee 480                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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| ggatggccat gttcccacag cctgagtggc tgccacctga tggctgatat agcaaaggcc 480 ttaggaaaag cagatggccc ttggccctac ctttttgtta gaagaactga tgttccatgt 540                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            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| rlaqqaaaaq caqalqqccc tiqqccciac cillicqtia qaaqaaciqa tqilccaiqi 540                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  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 | ens<br>gtgca<br>agggt<br>attct<br>cagaa<br>agaat<br>tgcgt        | aa ca<br>ta to<br>ta go<br>aa go<br>ta to<br>go co                                     | actg<br>jeget<br>jttge<br>agec<br>jtgee<br>jaggt                            | tgct<br>gcct<br>caag<br>agga<br>aagg                                         | acaaat<br>tegget<br>aggeca<br>teacea<br>caggae<br>ccaaac<br>cageca                                | ctcc<br>acca<br>tcca<br>aagc<br>tggc<br>ccaa                                         | aato<br>cagg<br>gggg<br>tcao<br>tcao<br>cctt                                         | cato<br>gecat<br>gactt<br>ctcac<br>atgac<br>cacco                                   | ct i<br>gg i<br>gag o<br>gca a                                                                                                                                                                                                                                                                                                       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| cetgeagega gtgaggttgg tggetgtgee eccageteet ggeacacect egcagaggtg 600                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  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 | ens gtgca agggt attct cagaa agaat tgcgt                          | aa ca<br>ta to<br>ta go<br>ta go<br>ga go                                              | actg<br>reget<br>rtge<br>agec<br>ragac<br>raggt                             | tgct<br>gcct<br>caag<br>agga<br>aagg<br>ggac                                 | acaaat<br>tegget<br>aggeca<br>teacea<br>caggae<br>caaae<br>cageca                                 | ctcc<br>acca<br>tcca<br>aagc<br>tggc<br>ccaa                                         | aato<br>cago<br>gggg<br>tcao<br>tcao<br>cctt                                         | cate<br>yecat<br>yactt<br>etcae<br>atgae<br>cace<br>etgat                           | cc icc icc icc icc icc icc icc icc icc                                                                                                                                                                                                                                                                                               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| actggttgct ctttgagccc tcttagcctt gcccagcatg cacaagcctc agtgctacta 660                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  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 | ens gtgca agggt attct cagaa agaat tgcgt ccaca                    | aa ca<br>ta to<br>ta go<br>ta go<br>to to<br>ga go<br>ag co                            | actg<br>jeget<br>jttge<br>agee<br>jtgee<br>aggt<br>tgag                     | tgct<br>gcct<br>caag<br>agga<br>aagg<br>ggac<br>tggc                         | acaaat<br>tegget<br>aggeea<br>teacea<br>caggae<br>caaae<br>cageea<br>tgeeae                       | ctcc<br>acca<br>tcca<br>aagc<br>tggc<br>ccaa<br>ctga<br>gtta                         | aato<br>cago<br>gggg<br>tcao<br>tcao<br>cctt<br>tggo<br>gaag                         | cato<br>gecat<br>gactt<br>etcac<br>atgac<br>cacco<br>etgat                          | cc i<br>gg i<br>gag d<br>gca a<br>gag i<br>at a                                                                                                                                                                                                                                                                                      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| ctgtgctaca aatggagcca tataggggaa acgagcagcc atctcaggag caaggtgtat 720                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  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sapi<br>ttca<br>gage<br>cacg<br>acatg<br>tetg<br>gttc<br>caga<br>gtga<br>ettt          | ens gtgca agggt attct cagaa agaat tgcgt ccaca tggcc ggttc        | aa ca<br>ta to<br>ta go<br>ta go<br>to to<br>go to<br>too to                           | aactg<br>geget<br>gtgee<br>agee<br>gaggt<br>etgag<br>ggee<br>ggetg          | tgct<br>gcct<br>caag<br>agga<br>aagg<br>ggac<br>tggc<br>ctac<br>tgcc         | acaaat<br>tegget<br>aggeca<br>teacea<br>caggae<br>caace<br>tgecae<br>cttttt<br>cecage             | ctcc<br>acca<br>tcca<br>aagc<br>tggc<br>ccaa<br>ctga<br>gtta<br>tcct                 | aato<br>cago<br>gggg<br>tcac<br>tcac<br>cctt<br>tggc<br>gaag<br>ggca<br>caca         | ccate<br>gccat<br>gactt<br>ctcae<br>atgae<br>cace<br>gaact<br>gaact                 | ged to the second of the secon | gaaac<br>ceage<br>cette<br>cage<br>ceae<br>ceae<br>cgtte<br>cgcae                 | caagca<br>ggctcc<br>aaggag<br>ctgtgg<br>gtgtta<br>gccacc<br>ggaagt<br>aaggcc<br>ccatgt<br>gaggtg           | 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| getgeetttg ggggeteeag teettgeete aagggtetta tgteactgtg ggettettgg 780 ttgeeaagag geagaccata g 801                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      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 | ens gtgca agggt attct cagaa agaat tgcgt ccaca cggttg             | aa ca<br>ta to<br>tt go<br>ta go<br>to tt<br>gg to<br>to to                            | actg<br>jeget<br>jttge<br>agee<br>jaggt<br>tgag<br>gee<br>geetg             | tgct<br>gcct<br>caag<br>agga<br>aagg<br>ggac<br>tggc<br>ctac<br>tgcc<br>cctt | acaaat<br>tegget<br>aggeea<br>teacea<br>caggeea<br>tgeeac<br>cttttt<br>cecage<br>acgage           | ctcc<br>acca<br>tcca<br>aagc<br>tggc<br>ccaa<br>gtta<br>tcct<br>agcc                 | aato                                                                                 | ccate<br>gccat<br>gactt<br>ctcae<br>atgae<br>cace<br>gaact<br>gaact<br>acae<br>cage | ct diagram of the control of the con | gaaac<br>ccage<br>cctte<br>cage<br>accae<br>ccae<br>cgtte<br>ccae<br>cgte<br>ccae | caagca<br>ggctcc<br>aaggag<br>ctgtgg<br>gtgtta<br>gccacc<br>ggaagt<br>ccatgt<br>gaggtg<br>ctacta           | 60<br>120<br>180<br>240<br>300<br>360<br>420<br>480<br>540<br>660<br>720               |     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| <210> 534                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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gctcaca gcagega                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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sapi<br>ttca<br>gage<br>acacg<br>acatg<br>tctg<br>gttc<br>caga<br>gtga<br>cttt<br>aatg | ens gtgca agggt attct cagaa agaat tgcgt ccaca tggcc cgagcc gagcc | aa ca<br>ta to<br>ta go<br>ta go<br>ta go<br>ga go<br>ta ta<br>ga ta<br>ta ta          | aactg<br>jeget<br>jtgee<br>agee<br>jaggt<br>tgag<br>ggetg<br>ttagg<br>ttagg | tgct<br>gcct<br>caag<br>agga<br>aagg<br>ggac<br>tggc<br>ctac<br>tgcc<br>cctt | acaaat<br>tegget<br>aggeea<br>teacea<br>caggeea<br>tgeeac<br>cttttt<br>cecage<br>acgage           | ctcc<br>acca<br>tcca<br>aagc<br>tggc<br>ccaa<br>gtta<br>tcct<br>catg<br>agcc<br>ctta | aato<br>cagg<br>gggg<br>tcac<br>tcaa<br>cctt<br>tggc<br>gaag<br>ggca<br>caca<br>atct | ccate<br>gccat<br>gactt<br>ctcae<br>atgae<br>cace<br>gaact<br>gaact<br>acae<br>cage | ct diagram of the control of the con | gaaac<br>ccage<br>cctte<br>cage<br>accae<br>ccae<br>cgtte<br>ccae<br>cgte<br>ccae | caagca<br>ggctcc<br>aaggag<br>ctgtgg<br>gtgcacc<br>ggaagt<br>aaggcc<br>caggtg<br>gaggtg<br>tacta<br>gtgtat | 60<br>120<br>180<br>240<br>300<br>420<br>480<br>540<br>600<br>660<br>720               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 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| <211> 266                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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<th>aactg<br/>jeget<br/>jtgee<br/>agee<br/>jaggt<br/>tgag<br/>tgage<br/>ttagg<br/>ttagg</th> <th>tgct<br/>gcct<br/>caag<br/>agga<br/>aagg<br/>ggac<br/>tggc<br/>ctgc<br/>cctt</th> <th>acaaat<br/>tegget<br/>aggeea<br/>teaegae<br/>cageea<br/>tgeeae<br/>tgeeag<br/>eccage<br/>acgage<br/>aagggt</th> <th>etce<br/>acca<br/>teca<br/>aage<br/>etgge<br/>ectga<br/>etcet<br/>catg<br/>agec<br/>ecta</th> <th>aato<br/>cago<br/>gggg<br/>tcao<br/>tcao<br/>cctt<br/>tggo<br/>gaag<br/>ggca<br/>caca<br/>atot</th> <th>ceate<br/>yecat<br/>yactt<br/>yactt<br/>yacte<br/>yaact<br/>yaact<br/>yaacte<br/>yaacte</th> <th>ged in the second secon</th> <th>gaaaq<br/>cagga<br/>catto<br/>cagca<br/>cagca<br/>agca<br/>agta<br/>caagg</th> <th>caagca<br/>ggctcc<br/>aaggag<br/>ctgtgg<br/>gtgtta<br/>ggaagt<br/>aaggcc<br/>catgt<br/>gaggtg<br/>ctacta<br/>gtgtat</th> <th>60<br/>120<br/>180<br/>240<br/>300<br/>360<br/>420<br/>480<br/>540<br/>660<br/>720<br/>780<br/>801</th> <th></th> <th></th> <th></th>                             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tgct<br>gcct<br>caag<br>agga<br>aagg<br>ggac<br>tggc<br>ctgc<br>cctt         | acaaat<br>tegget<br>aggeea<br>teaegae<br>cageea<br>tgeeae<br>tgeeag<br>eccage<br>acgage<br>aagggt | etce<br>acca<br>teca<br>aage<br>etgge<br>ectga<br>etcet<br>catg<br>agec<br>ecta      | aato<br>cago<br>gggg<br>tcao<br>tcao<br>cctt<br>tggo<br>gaag<br>ggca<br>caca<br>atot | ceate<br>yecat<br>yactt<br>yactt<br>yacte<br>yaact<br>yaact<br>yaacte<br>yaacte     | ged in the second secon | gaaaq<br>cagga<br>catto<br>cagca<br>cagca<br>agca<br>agta<br>caagg                | caagca<br>ggctcc<br>aaggag<br>ctgtgg<br>gtgtta<br>ggaagt<br>aaggcc<br>catgt<br>gaggtg<br>ctacta<br>gtgtat  | 60<br>120<br>180<br>240<br>300<br>360<br>420<br>480<br>540<br>660<br>720<br>780<br>801 |                                                                                                                                                                                                                                                               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| <211> 266                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | <210 213</213</213</214</215</215</216</th <th>290  2&gt; 533  3&gt; Homo  3&gt; Homo  3&gt; Grace ago  3 Grace ago  4 Grace ago  5 Grace ago  5 Grace ago  6 Grace ago  7 Grace ago</th> <th>sapi<br/>ttca<br/>gage<br/>acat<br/>tctg<br/>gtca<br/>gtga<br/>cttt<br/>aatg<br/>gggg<br/>gcag</th> <th>ens gtgca agggt attct cagaa tctgc ccaca tggttc gagcc ccacat</th> <th>aa ca<br/>ta to<br/>ta go<br/>ta go<br/>ta go<br/>ta go<br/>ta to<br/>ta go<br/>ta ta<br/>ag to</th> <th>aactg<br/>jeget<br/>jtgee<br/>agee<br/>jaggt<br/>tgag<br/>tgage<br/>ttagg<br/>ttagg</th> <th>tgct<br/>gcct<br/>caag<br/>agga<br/>aagg<br/>ggac<br/>tggc<br/>ctgc<br/>cctt</th> <th>acaaat<br/>tegget<br/>aggeea<br/>teaegae<br/>cageea<br/>tgeeae<br/>tgeeag<br/>eccage<br/>acgage<br/>aagggt</th> <th>etce<br/>acca<br/>teca<br/>aage<br/>etgge<br/>ectga<br/>etcet<br/>catg<br/>agec<br/>ecta</th> <th>aato<br/>cago<br/>gggg<br/>tcao<br/>tcao<br/>cctt<br/>tggo<br/>gaag<br/>ggca<br/>caca<br/>atot</th> <th>ceate<br/>yecat<br/>yactt<br/>yactt<br/>yacte<br/>yaact<br/>yaact<br/>yaacte<br/>yaacte</th> <th>ged in the second secon</th> <th>gaaaq<br/>cagga<br/>catto<br/>cagca<br/>cagca<br/>agca<br/>agta<br/>caagg</th> <th>caagca<br/>ggctcc<br/>aaggag<br/>ctgtgg<br/>gtgtta<br/>ggaagt<br/>aaggcc<br/>catgt<br/>gaggtg<br/>ctacta<br/>gtgtat</th> <th>60<br/>120<br/>180<br/>240<br/>300<br/>360<br/>420<br/>480<br/>540<br/>660<br/>720<br/>780<br/>801</th> <th></th> <th></th> <th></th> | 290  2> 533  3> Homo  3> Homo  3> Grace ago  3 Grace ago  4 Grace ago  5 Grace ago  5 Grace ago  6 Grace ago  7 Grace ago  | sapi<br>ttca<br>gage<br>acat<br>tctg<br>gtca<br>gtga<br>cttt<br>aatg<br>gggg<br>gcag   | ens gtgca agggt attct cagaa tctgc ccaca tggttc gagcc ccacat      | aa ca<br>ta to<br>ta go<br>ta go<br>ta go<br>ta go<br>ta to<br>ta go<br>ta ta<br>ag to | aactg<br>jeget<br>jtgee<br>agee<br>jaggt<br>tgag<br>tgage<br>ttagg<br>ttagg | tgct<br>gcct<br>caag<br>agga<br>aagg<br>ggac<br>tggc<br>ctgc<br>cctt         | acaaat<br>tegget<br>aggeea<br>teaegae<br>cageea<br>tgeeae<br>tgeeag<br>eccage<br>acgage<br>aagggt | etce<br>acca<br>teca<br>aage<br>etgge<br>ectga<br>etcet<br>catg<br>agec<br>ecta      | aato<br>cago<br>gggg<br>tcao<br>tcao<br>cctt<br>tggo<br>gaag<br>ggca<br>caca<br>atot | ceate<br>yecat<br>yactt<br>yactt<br>yacte<br>yaact<br>yaact<br>yaacte<br>yaacte     | ged in the second secon | gaaaq<br>cagga<br>catto<br>cagca<br>cagca<br>agca<br>agta<br>caagg                | caagca<br>ggctcc<br>aaggag<br>ctgtgg<br>gtgtta<br>ggaagt<br>aaggcc<br>catgt<br>gaggtg<br>ctacta<br>gtgtat  | 60<br>120<br>180<br>240<br>300<br>360<br>420<br>480<br>540<br>660<br>720<br>780<br>801 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                       |  |

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|                | )> 5  |            |             |           | ·     |          |                                       | •                                            | 1       |        |           |           |       |                      |            |   |
|----------------|-------|------------|-------------|-----------|-------|----------|---------------------------------------|----------------------------------------------|---------|--------|-----------|-----------|-------|----------------------|------------|---|
| Met            | Tyr   | Lys        | Leu         | Gln       | Cys   | Asn      | Asn                                   | Cys                                          | Ala     | Thr    | Asn       | Gly       | Ala   | Thr                  | Glu        |   |
|                |       |            |             | 5         | 1     |          | 7.                                    |                                              | 10      |        |           |           | 2     | 15                   |            |   |
|                |       |            |             |           | 11    |          |                                       | •                                            | ٠,      |        |           |           | •     |                      |            |   |
| Arg            | Lys   | Gln        | Ala         | Ala       | Gly   | Ser      | Gly                                   | Ala                                          | ·Gly    | Tyr    | Ala       | Leu       | Pro   | Ser                  | Ala        |   |
|                |       |            | 20          |           |       |          |                                       | 25                                           |         |        |           | • .       | . 30  |                      |            |   |
|                |       | •          |             | '         |       |          | ٠.                                    | -                                            | -       | • • •  |           |           |       | ٠.                   |            |   |
| Leu            | Gln   | Ser        | Met         | Pro       | Gln   | Gly      | Ser                                   | Tyr                                          | Ala     | Thr    | Ala       | Arg       | Phe.  | Leu                  | Val        |   |
|                |       | 35         | •           | • • •     |       |          | .: 40                                 | •                                            | :       |        |           | 45        |       |                      |            |   |
|                |       |            | 100         | ٠         |       |          | 1, 1                                  | ٠.                                           | . '     | 4      | 1 .       |           |       | . :                  | 1.0        |   |
| Ala            | Lys   | Arg        | Pro         | Thr       | Thr   | Gly      | His                                   | Leu                                          | Glu.    | Lys    | Glu       | Phe       | Met.  | Phe                  | His        |   |
|                | 50    |            |             |           | ٠,    | ុ55      |                                       |                                              |         |        | √ 60      | ·         | `.    | 55. J. C             |            |   |
|                |       | •          |             |           |       | , , , ,  |                                       | ٤,                                           | • • • • | 1      | : :       |           |       |                      |            | ٠ |
|                | Arg   | Гуs        | Gln.        | Pro       |       | Ser      | Pro                                   | Ser                                          | Arg     |        | Leu       | Gly       | Leu   | Leu                  | Trp        | • |
| 65             |       |            |             | •         | 70    |          |                                       |                                              |         | :.75   |           |           | · .   | *                    | 80         |   |
| _              | -     |            |             |           | ` :   | -:       |                                       | <u>.                                    </u> |         |        |           | _ * '     |       |                      |            | • |
| Pro            | Trp   | Pro        | Asp         |           | Glu   | Phe      | Val:                                  | Pro                                          |         | Gln    | Asp       | Lys       | Leu   |                      |            |   |
|                |       | •          |             | 85        | :     |          |                                       | 1. •                                         | 90      | ٠      |           |           |       | 95.                  |            |   |
| _              | _     |            |             |           |       | 4.       |                                       |                                              |         | _      |           | <br>      | _     |                      |            |   |
| Ser            | Ser   | 'Val       | "           | Val       | Pro   | Gln      |                                       |                                              | Ala     | Cys    | Gin       | Thr       | _     | Pro                  | Asn :      |   |
|                |       | •          | 100         |           |       |          |                                       | 105                                          |         | . '    |           |           | 110   |                      | ,          |   |
| _              |       |            |             |           | _ :   |          |                                       |                                              |         |        | 2 () .    | _         |       |                      |            |   |
| Trp            | ren   |            | GIU         | GIN       | Pro   | ALa      |                                       | ser                                          | ALa     | GLY    | val.      |           | ьeu:  | GTU                  | Glu        |   |
|                |       | 115        |             |           |       |          | 120                                   |                                              |         |        |           | 125       | 44.5  |                      |            |   |
| T7- 1          | 7     |            | D           | D         | m1    | T 0      | Dwa                                   | 0                                            | C7-     | c1     | Com       | C1        | m     |                      | <b>-</b>   |   |
| var            | 130   |            | Pro         | Pro       | THE   | 135      | PLO                                   | Ser                                          | GIII    | GTĀ    |           | GTA       | _     | PIO                  | Cys        |   |
|                | 130   |            |             |           |       | T32      |                                       |                                              |         |        | TAO       |           |       |                      | to jedno a |   |
| Sor            | uie   | Sor        | T.e.i       | Sar       | ·G] 🕶 | Cue      | Hic                                   | Lan                                          | Mot     | Δ1 a   | Δen       | Tla       | 7.1 a | T.tre                | Ala        |   |
| 145            | пто   | ner        | neu.        | Det       | 150   | Cyb.     | · III.                                | TIEU                                         | Hec     | 155    | nop       | 776       | ALC.  | цуз                  | 160        |   |
| 740            | · .   |            |             |           | 130   |          |                                       |                                              |         |        |           |           |       |                      | 100        |   |
| Len            | G] v  | Tivs       | Ala         | Agn       | Glv   | Pro      | Tro.                                  | Pro                                          | Tur     | Leu    | Phe       | Val.      | Ara   | Ara                  | Thr        |   |
|                | 0-1   |            |             | 165       | 01,   |          |                                       |                                              | 170     |        |           |           | 9     | 175                  |            |   |
|                |       |            |             |           |       |          |                                       |                                              |         |        |           |           |       |                      |            |   |
| Asp            | Val   | Pro        | Cys         | Pro       | Ala   | Ala      | Ser                                   | Glu                                          | .Val.   | Glv    | Glv       | Cvs       | Ala   | Pro                  | Ser        |   |
|                |       |            | 180         |           |       |          | -                                     | 185                                          |         | ١.,    |           |           | 190   |                      |            |   |
|                |       |            |             |           |       |          |                                       |                                              | -, 1    |        |           |           |       |                      | ٠ ـ        |   |
| Ser            | Trp   | His        | Thr         | Leu       | Ala   | Glu      | Val                                   | Thr                                          | Gly     | Cys    | Ser       | Leu       | Ser   | Pro                  | Leu        |   |
|                | _     | 195        | 1           |           |       |          | 200                                   |                                              | ·       | : -    | ٠.        | 205       |       |                      |            |   |
|                | •     |            | •           |           |       |          | •                                     | ÷                                            | ٠.      |        |           | ٠.        |       |                      |            |   |
| Ser            | Leu   | Ala        | Gln         | His       | Ala   | Gln      | Ala                                   | Ser                                          | Val     | Leu    | Leu       | Leu       | Cys'  | Tyr                  | Lys        | - |
|                | 210   |            |             |           |       | 215      |                                       | 4                                            | ٠. :    | •      | 220       | i         |       | , 18 ju              |            |   |
|                |       |            |             | •         |       | ,        |                                       |                                              |         | ·.     | ·         |           | ٠,    |                      |            | • |
| $\mathtt{Trp}$ | Ser   | His        | Ile         | Gly       | Glu   | Thr      | Ser                                   | Ser                                          | His     | Leu    | Arg       | Ser       | Lys   | Val:                 | Tyr        | • |
| 225            |       | ·          |             | : '       | 230   |          | • .                                   |                                              |         | 235    | 24.5      |           | . :   | 1                    | 240        | ۲ |
|                |       | . *        |             | ٠.        | •     | <i>.</i> |                                       |                                              | ; ·     |        | 1         | is in the | 202 2 |                      |            |   |
| Ala            | Ala   | Phe        |             |           |       |          |                                       |                                              |         |        |           |           |       |                      | Leu        |   |
|                |       |            |             | 245       | · .   |          | · · · · · · · · · · · · · · · · · · · | *:                                           | 250     | . ) T  | \$5.7 × 5 |           | :     | 255                  | 1. 1       |   |
|                |       |            |             | 100       | •     | • • •    |                                       | 1                                            | . : :   | 4 23   | , ':,     | • • • •   |       |                      |            |   |
| $\mathtt{Trp}$ | Ala   | Ser        | Trp         | Leu       | Pro   | Arg      | Gly                                   | Arg:                                         | Pro     |        | · 2 7:    | 1 1       | .5    |                      |            |   |
|                | •     | <b>3</b> ( | 260         | . 15      | 1     |          |                                       | 265                                          |         | ::     |           | •         | 2.2   | $v \in \mathfrak{J}$ |            | : |
|                |       |            |             | 4 .       | . :   | •        | : 1                                   |                                              | ` }· '' |        | K D       | ·         |       |                      | 1.7.3      | ٠ |
|                |       |            | : .         |           |       |          |                                       | j -                                          |         | i said |           |           | : :   | 76 i .               |            |   |
| <210           | )> 53 | 35         | •           | · · · · . | -     |          | ٠.                                    | 2 1 H                                        | ··· ··  | 100    | • •       | 2.70      | 1 1 1 | 2                    |            |   |
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| <212           | :> Dì | A.         | , at a      | • •       | ::: : |          | * • • • .                             |                                              | •       | 3.5    | 2         | 11 3 J    | •     | .* :                 |            |   |
| <213           | 5> Hc | omo s      | sapie       | ns        |       |          | . :                                   |                                              | · 2.1   | j      |           | . :       |       | ·                    | • • •      |   |

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<sup>&</sup>lt;211> 1228

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens

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|------------|------------|-----------|------------|-------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Pro        | Glu<br>50  | Asp       | Arg        | Ser         | Gln        | 55         |            |            | Glu        | - 1m       | 60         | 26.7       | 130        |            | Trp        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Asp<br>65  | Lys        | Glu       | Val        | Leu         | 70         | Ala        | Glu        | Asn        | Asp        | Ala        | Gln        | Lys        | Pro        | Ser        | Leu<br>80  | in the second second                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Thr        | Arg        | Ala       |            | 85          | Lvs        | Cys        | Tyr        | Trp        | Lvs        | Ser        | Tyr        | Leu        | Val        | Leu        | Gly        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Ile        |            |           | Leu        | Ile         | Glu        | Glu        | Ser        | Ala        | , 1, 11 4. | Val        | Ile        | Gln        | Pro        | Ile        | Phe        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Leu        | Gly        | Lys       | Ile        | Ile         | Asn        | Tyr        | Phe        | Glu        | Asn        | Tyr        | Asp        | Pro        | Met        | Asp        | Ser        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Val        | Ala        | Leu       | Asn        | Thr         | Ala        | Tyr        | Ala        | Tyr        | Ala        | Thr        | Val        | Leu        | Thr        | Phe        | Суз        | and the first of the first                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Thr<br>145 | Leu        | Ile       | Leu        | Ala         | 11e-       | Leu        | His        | His        | Leu        | Tyr<br>155 | Phe        | Tyr        | His        | Val        | Gln '      | and the state of t    |
| Cys        | Ala        | G1y       | Met        | Arg         | Leu        | Arg        | Val        | Ala        | Met        | Cys        | His        | Met        | Ile        | Tyr        | Arg        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Lys        | Alá        | Leu       | Arg<br>180 | Leu         | Ser        | Asn        | Met        | Ala<br>185 | Met        | Gly        | Lys        | Thr        | Thr<br>190 | Thr        | Gly        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Gln        |            | 195       | Asn        | Leu         | Leu        | Ser        | Asn<br>200 | Asp        | Val        | Asn        | Lys        | Phe<br>205 | Asp        | Gln        | Val        | 1일 회원(경기원 시간 기간<br>- 1일(원) 원원 기간 기간                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Thr        | Val<br>210 |           | Leu        | His         | Phe        | Leu<br>215 | Trp        | Ala        | Gly        | Pro        |            | Gln        |            | Ile        | Ala        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Val<br>225 |            | Ala       |            | Leu         | Trp<br>230 | Met        | Glu        | Ile        | Gly.       | 11e<br>235 | Ser        | Cys        | Leu        | Ala        | Gly<br>240 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Met        |            |           | Leu        | Ile:<br>245 | Ile        | Leu<br>!   | Leu        | Pro        |            | Gln        | Ser        |            | Phe        | Gly<br>255 | Lys        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Leu        |            | 1. 1.     | Ser<br>260 | Leu         | Arg        | Ser        | Lys        | Thr<br>265 | Ala        | Thr        |            |            | Asp<br>270 | Ala        | Arg        | estados de la composição de la composição<br>La composição de la composição d |
| Ile        | Arg        |           | Met        |             |            |            |            |            |            |            |            | Ile<br>285 | Ile        | Lys        | Met        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Tyr        | Ala<br>290 | Trp       | G1u        | Lys         | Ser        | Phe<br>295 | Ser        | Asn        | Leu        | Ile        | Thr<br>300 | Asn        | Leu        | Arg        |            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Lys<br>305 | Glu        | Ile       | Ser        |             | 310        |            |            |            |            | 315        |            |            |            |            | Asn<br>320 | ew ee                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Leu        | Ala        | Ser       | Phe        | Phe<br>325  | Ser        | Ala        | Ser        | Lys        | Ile 330    | Ile        | Val        | Phe        | Val        | Thr<br>335 | Phe        | n egy x of the second                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Thr        | Thr        | Tyr       | Val        |             |            |            |            |            |            |            |            |            |            |            |            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |

|            |            |            | 340        |            | •          |            |            | 345        | 1          |            |            |            | 350        |            |            |            |              |       |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|--------------|-------|
| Val        | Ala        | Val<br>355 | Thr        | Leu        | Tyr        | Gly        | Ala<br>360 | Val        | Arg        | Leu        | Thr        | Val<br>365 | Thr        | Leu        | Phe        |            |              | •     |
| Phe        | Pro<br>370 | Ser        | Ala        | Ile        | Glu        | Arg<br>375 | Val        | Ser        | Glu        | Ala        | Ile<br>380 | Val        | Ser        | Ile        | Arg        | *.         | ;            | . •   |
| Arg<br>385 | Ile        | Gln        | Thr        | Phe        | Leu<br>390 | Leu        | Leu        | Asp        | Glu        | I1e<br>395 | Ser        | Gln        | Arg        | Asn        | Arg<br>400 | :          |              |       |
| Gln        | Leu        | Pro        | Ser        | Asp<br>405 | Gly        | Lys        | Lys        | Met        | Val<br>410 | His        | Val        | Gln        | Asp        | Phe 415    | Thr        | •          |              |       |
| Ala        | Phe        | Trp        | Asp<br>420 | Lys        | ,Ala       | Ser        | Glu        | Thr<br>425 | Pro        | Thr        | Leu        | Gln        | Gly<br>430 | Leu        | Ser        |            |              |       |
| Phe        | Thr        | Val<br>435 | Arg        | Pro        | Gly        | Glu        | Leu<br>440 | Leu        | Ala        | Val        | Val        | Gly<br>445 | Pro        | Val        | Gly        |            |              |       |
| Ala        | Gly<br>450 | Lys        | Ser        | Ser        | Leu        | Leu<br>455 | Ser        | Ala        | Val        | Leu        | Gly<br>460 | Glu        | Leu        | Ala        | Pro        | د بر       |              | .,, . |
| Ser<br>465 | His        | Gly        | Leu        | Val        | Ser<br>470 | Val        | His        | Gly        | Arg        | 11e<br>475 | Ala        | Tyr        | Val        | Ser        | Gln<br>480 |            |              | 2     |
| Gln        | Pro        | Trp        | Val        | Phe 485    | Ser        | Gly        | Thr        | Leu        | Arg<br>490 | Ser        | Asn        | Ile        | Leu        | Phe<br>495 | Gly        |            |              | 1.00  |
| Lys        | Lys        | Tyr        | Glu<br>500 | Lys        | Glu        | Arg        | Tyr        | Glu<br>505 | Lys        | Val        | Ile        | Lys        | Ala<br>510 | Cys        | Ala        | 1          | ٠.           | :     |
| Leu        | Lys        | Lys<br>515 | Asp        | Leu        | Gln        | Leu        | Leu<br>520 | Glu        | Asp        | ĠŢÃ        | Asp        | Leu<br>525 | Thr        | Val        | Ile        |            | -            | •     |
| Gly        | Asp<br>530 | Arg        | Gly        | Thr        | Thr        | Leu<br>535 | Ser        | Gly        | Gly        | Gln        | Lys<br>540 | Ala        | Arg        | Val        | Asn        | •          | , <u>.</u> ' | •     |
| Leu<br>545 | Ala        | Arg        | Ala        | Val        | Tyr<br>550 | Gln        | Asp        | Ala        | Asp        | 11e<br>555 | Tyr        | Leu        | Leu        | Asp        | Asp<br>560 |            |              | ·     |
| Pro        | Leu        | Ser        | Ala        | Val<br>565 | Asp        | Ala        | Glu        | Val        | Ser<br>570 | Arg        | His        | Leu        | Phe        | Glu<br>575 | Leu        |            |              | )     |
| Суз        | Ile        | Cys        | Gln<br>580 | Ile        | Leu        | His        | Glu        | Lys<br>585 | Ile        | Thr        | Ile        | Leu        | Val<br>590 | Thr        | His        | · .        | , "4         | Sit   |
| Gln        | Leu        | Gln<br>595 | Tyr        | Leu        | Lys        | Ala        | Ala<br>600 | Ser        | Gln        | Ile        | Leu        | Ile<br>605 | Leu        | Lys        | Asp        | -2.29<br>- | . 93         | iş.   |
| Gly        | Lys<br>610 | Met        | Val        | Gln        | Lys        | Gly<br>615 | Thr        | Tyr        | Thr        | Glu        | Phe<br>620 | Leu        | ГЛЗ        | Ser        | Gly        |            |              | .•    |
| Ile<br>625 | Asp        | Phe        | Gly        | Ser        | Leu<br>630 | Leu        | Lys        | Lys        | Asp        | Asn<br>635 | Glu        | Glu        |            | Glu        | Gln<br>640 | ,          | •            | **    |
| Pro        | Pro        | Val        | Pro        | Gly<br>645 | Thr        | Pro        | Thr        | Leu        | Arg<br>650 | Asn        | Arg        | Thr        | Phe        | Ser<br>655 | Glu        |            | .* *         | •     |

|   |            |            |            |            |                  |            |            |            |               | •          |             |            |              |             |            |            |       |                                         |       |
|---|------------|------------|------------|------------|------------------|------------|------------|------------|---------------|------------|-------------|------------|--------------|-------------|------------|------------|-------|-----------------------------------------|-------|
|   | Ser        | Ser        | Val        | Trp<br>660 | Ser              | Gln        | Gln        | Ser        | Ser<br>665    | Arg        | Pro         | Ser        | Leu          | Lys<br>670  | Asp        | Gly        |       |                                         |       |
|   | Ala        | Leu        | Glu<br>675 | Ser        | Gln <sub>j</sub> | Asp        | Thr        | Glu<br>680 |               | Val        | Pro         | Val        | Thr<br>685   | Leu         | Ser        | Glu        |       |                                         |       |
|   | Glu        | Asn<br>690 | Arg        | Ser        | Glu              | Gly        | Lys<br>695 | Val        | Gly           | Phe        | Gln         | Ala<br>700 | Tyr          | Lys         | Asn        | Tyr        | ,~ ·  | •                                       |       |
|   | Phe<br>705 | Arg        | Ala        | Gly        | Ala              | His<br>710 | Trp        | Ile        | Val           | Phe        | 715         | Phe        | Leu          | Ile         |            | Leu<br>720 |       | •                                       |       |
|   | Asn        | Thr        | Ala        | Aļa        | Gln<br>725       | ,Val       | Ala        | Tyr        | Val           | Leu<br>730 | Gln         | Asp        | Trp          | Trp         | Leu<br>735 | Ser        |       |                                         |       |
|   | Tyr        | Trp        | Ala        | Asn<br>740 |                  | Gln        | Ser        | 1          | Leu<br>745    | Asn        | Val         | Thr        | , 21 k       | Asn<br>750  | Gly        | Gly        |       |                                         |       |
|   | Gly        | Asn        | Val<br>755 | Thr        | Glu              | Lys        | Leu        | Asp<br>760 | Leu<br>?      | Asn        | Trp         | Tyr        | Leu<br>765   | Gly         | Ile        | Tyr        |       |                                         | 1 .   |
|   | Ser        | Gly<br>770 | Leu        | Thr        | .Val             | Ala        | Thr<br>775 | Val        | Leu           | Phe        | Gly         | 11e<br>780 | Ala          | Arg         | Ser        | Leu        |       |                                         |       |
|   | Leu<br>785 | Val        | Phe        | Tyr        | Val              | Leu<br>790 | Val        | Asn        | Ser           | Ser        | Gln<br>795  | Thr        | Leu          | His         | Asn        | Lys<br>800 |       |                                         |       |
|   | Met        | Phe        | Glu        | Ser        | 11e<br>805       | Leu        | Lys        | Ala        | Pro           | Val<br>810 |             | Phe        |              |             |            | Asn        | · • . |                                         |       |
|   | Pro        | Ile        | Gly        | Arg<br>820 | Ile              | Leu        | Asn        | Arg        | Phe<br>825    | Ser        | Lys         | Asp        | Ile          | Gly<br>830  |            |            | :     |                                         |       |
|   | Asp        | Asp        | Leu<br>835 | Leu        | Pro              | Leu        | Thr        | Phe 840    |               | Asp        | Phe         | Ile        | Gln<br>845   | Thr         | Leu        | Leu<br>J   |       |                                         |       |
|   | Gln        | Val<br>850 | Val        | Gly        | Val              | Val        | Ser<br>855 | Val        |               | Val        | Ala         | Val<br>860 | Ile          | Pro         | Trp        | Ile<br>::  |       | -                                       |       |
|   | Ala<br>865 | Ile        | Pro        | Leu        | Val              | Pro<br>870 | Leu        | Gly<br>∵   | Ile           | Ile        | Phe<br>875  | Ile        | Phe          | Leu         |            | Arg<br>880 | . :   |                                         |       |
|   | Tyr        | Phe        | Leu        | Glu        | Thr<br>885       | Ser        | Arg        | Asp        | Val           | Lys<br>890 | Arg         | Leu        | Glu          | Ser         | Thr<br>895 | <b>Thr</b> |       |                                         |       |
|   | Arg        | Ser        | Pro        | Val<br>900 | Phe              | Ser        | His        | Leu        | Ser<br>905    | Ser        | Ser         | Leu        | Gln          |             | Leu        | Trp        |       |                                         |       |
|   | Thr        | Ile        | Arg<br>915 | Ala,       | Tyr              | Lys        | Ala        | Glu<br>920 | Glu<br>(7.55) | Arg        | Cys<br>I, I | Gln        | Glu<br>925   | Leu<br>egil | Phe        | Asp        | ξĵ    | · • • • • • • • • • • • • • • • • • • • |       |
| • | Ala        | His<br>930 | Gln        | Asp        | Leu              | His        | Ser<br>935 | ij÷,       | Ala           | Trp        | Phe         | Leu<br>940 | Phe<br>o.tri | Leu<br>Aud  | Thr        | Thr        | ಕರ್ಗ  |                                         | 5 i., |
|   | S r<br>945 | Arg        | Trp        | Phe        | Ala              | Val<br>950 | Arg        | Leu        | Asp           | Ala        | Ile<br>955  | Cys        | Ala          | Met         | Phe        | Val<br>960 | 137   | কর্ম্                                   |       |
|   |            |            |            |            |                  |            |            |            |               | •          |             |            |              |             |            |            |       |                                         |       |

| Ile          | Ile         | Val         | Ala         | Phe<br>965  | Gly            | Ser                                   | Leu         | Ile         | Leu<br>970  | Ala         | Lys         | Thr                                   | Leu         | Asp<br>975   | Ala         |          | :  |                |
|--------------|-------------|-------------|-------------|-------------|----------------|---------------------------------------|-------------|-------------|-------------|-------------|-------------|---------------------------------------|-------------|--------------|-------------|----------|----|----------------|
| Gly          | Gln         | Val         | Gly<br>980  | Leu         | Ala            | Leu                                   | Ser         | Tyr<br>985  | Ala         | Leu         | Thr         | Leu                                   | Met<br>990  | Gly          | Met         | ,<br>,   | ÷  | ٠,             |
| Phe          | Gln<br>·    | Trp<br>995  | Cys         | Val         | Arg            | Gln                                   | Ser<br>1000 |             | Glu         | Val         | Glu         | Asn<br>1005                           |             | Met          | Ile         |          |    |                |
| Ser          | Val<br>1010 |             | Arg         | Val         | Ile            | Glu<br>1015                           | -           | Thr         | Asp         | Leu         | Glu<br>1020 |                                       | <b>Glu</b>  | Ala          | Pro         |          |    |                |
| Trp<br>1025  |             | Tyr         | Gln         | Lys         | Arg<br>1030    |                                       | Pro         | Pro         | Ala         | Trp<br>1035 |             | His                                   | G1u         | Gly          | Val<br>1040 | ٠,       |    |                |
| Ile          | Ile         | Phe         | Asp         | Asn<br>1045 |                | Asn                                   | Phe         | Met         | Tyr<br>105  |             | Pro         | Gly                                   | Gly         | Pro<br>105   | _           |          |    |                |
| Val          | Leu         | Lys         | His<br>1060 |             | Thr            | Ala                                   | Leu         | Ile<br>106  | Lys         | Ser         | Gln         | Glu                                   | Lys<br>1070 | _            | Gly         |          |    |                |
| Ile          | Val         | Gly<br>1075 | Arg         | Thr         | Gly            | Ala                                   | Gly<br>1080 |             | Ser         | Ser         | Leu         | 1085                                  |             | Ala          | Leu         |          |    |                |
| Phe          | Arg<br>1090 |             | Ser         | Glu         | Pro            | Glu<br>109                            | _           | Lys         | Ile         | Trp         | Ile<br>1100 |                                       | Lys         | Ile          | Leu         | : *      |    |                |
| Thr<br>1105  |             | Glu         | Ile         | Gly         | Leu<br>1110    |                                       | Asp         | Leu         | Arg         | Lys<br>1115 |             | Met                                   | Ser         | Ile          | Ile<br>1120 | :        |    | ٠              |
| Pro          | Gln         | Glu         | Pro         | Val<br>1125 |                | Phe                                   | Thr         | Gly         | Thr<br>1130 |             | Arg         | Lys                                   | Asn         | Leu<br>1135  |             |          |    |                |
| Pro          | Phe         | Asn         | Glu<br>1140 |             | Thr            | Asp                                   | Glu         | Glu<br>1145 | _           | Trp         | Asn         | Ala                                   | Leu<br>1150 | _            | Glu         |          |    | e <sup>r</sup> |
| Val          | Gln         | Leu<br>1155 | Lys         | Glu         | Thr            | Ile                                   | Glu<br>1160 |             | Leu         | Pro         | Gly`        | Lys<br>1165                           |             | Asp          | Thr         |          |    | · 18           |
| Glu          | Leu<br>1170 |             | Glu         | Ser         | Gly            | Ser<br>1175                           |             | Phe         | Ser         | Val         | Gly<br>1180 |                                       | Arg         | Gln          | Leu         | 7 1 4    |    | 5715           |
| Val<br>1185  |             | Leu         | Ala         | Arg         | 1190           | Ile                                   | Leu         | Arg         |             |             | -           |                                       |             |              | Ile<br>1200 |          |    | i Kai          |
| Asp          | Glu         | Ala         |             | Ala         | Asn            | Val                                   | Asp         | Pro         | Arg         |             | Asp         | Glu                                   |             | Ile<br>1215  | Gln         |          |    |                |
| Lys          | Lys         | Ser         |             | Arg         |                |                                       |             | Thr<br>1225 | Ala         | Pro         | Cys         |                                       | r.          |              |             | 444      |    |                |
| <210<br><211 | > 12        | 61          | •           |             | 1 = 1<br>1 = 1 | · · · · · · · · · · · · · · · · · · · |             |             |             |             |             | e e e e e e e e e e e e e e e e e e e |             |              |             | : *<br>: |    |                |
| <212<br><213 |             |             | sapie       | _           | ,              | · We                                  | 544         |             |             | ÷           | -           | -                                     | •           | ٠ <u>.</u> • |             |          | •  |                |
| <400         | > 53        | 8           | _           | ;           | 1 1.5          |                                       | :           |             | y • •       |             |             |                                       |             | ٠.           | . • • •     |          | ŷ. |                |

Met Tyr Ser Val Leu Pro Glu Asp Arg Ser Gln His Leu Gly Glu Glu

|            |            |            | ٠,         | 5          | r .        |             |            |           | <b>1.0</b> |           | ٠.         |            |            | 15         |               |                       | •        |
|------------|------------|------------|------------|------------|------------|-------------|------------|-----------|------------|-----------|------------|------------|------------|------------|---------------|-----------------------|----------|
| Leu        | Gln        | GЉ         | Phe<br>20  | Trp        | Asp        | <b>r</b> À2 | Glu        | Val<br>25 | Leu        | Arg       | Ala        | Glu        | Asn<br>30  | Asp        | Ala           |                       |          |
| G1n        | ГÀЗ        | Pro<br>35  | Ser        | Leu        | Thr        | Arg         | Ala<br>40  | Ile       | Ile        | Lys       | Суз        | Tyr<br>45  |            | Lys        | Ser           | at to sale            |          |
| Tyr        | Leu<br>50  | Val        | Leu        | Gly        | Ile        | Phe<br>55   | Thr        | Leu       | Ile        |           | Glu<br>60  | Ser        | Ala        | ГЛЗ        |               |                       | `\<br>`\ |
| Ile<br>65  | Gln        | Pro        | Ile        | Phe        | Ļeu<br>70  | Gly         | Lys        | Ile       | Ile        | Asn<br>75 | Tyr        | Phe        | Glu        | Asn        | Tyr<br>80     | venia.<br>Promoti     |          |
| Asp        | Prœ        | Met        | Asp        |            |            |             |            |           |            |           |            |            |            |            | I             | j del sou             | ,        |
| Val        | Leu        | Thr        | Phe<br>100 |            | Thr        |             |            |           |            |           |            |            |            | Leu        |               | V.7 4*                | , .      |
| Phe        | Tyr        | His<br>115 | Val        |            |            |             |            |           |            |           |            |            |            |            |               |                       | yk y     |
| His        | Met<br>130 | Ile        | Tyr        | _          | Lys<br>Vo  | Ala<br>135  | Leu        | Arg       | Leu        | Ser       | Asn<br>140 | Met        | Ala        | Met        | Gly           | ੇ<br>ਹੋਵਾਂ ਨ<br>ਹੋਵਾਂ |          |
| Lys<br>145 | Thr        | Thr        | Thr        | Gly        | Gln<br>150 |             | Val        | Asn       |            |           |            | Asn        |            |            | Asn<br>3160 " |                       | į        |
| Lys        | Phe        | Asp        | Gln        | Val<br>165 | Thr        | Val         | Phe        | Leu       | His<br>170 | Phe       | Leu        | Trp        | Ala        | Gly<br>175 | Pro           | red a                 | ı, a     |
| Leu        | Gln        | Ala        | Ile<br>180 |            |            | Thr         |            |           | Leu        |           | Met        | Glu        | Ile<br>190 | Gly        | Ile           | 9 . T                 | : *      |
| Ser        | Cys        | Leu<br>195 | Ala        | Gly        | Met        |             |            |           | Ile<br>?   |           |            | Leu<br>205 | Pro        | Leu        | Gln           |                       |          |
| Ser        | Cys<br>210 | Phe        | Gly        | Lys        | Leu        | Phe 215     | Ser        | Ser       | Leu        |           | Ser<br>220 |            | Thr        | Ala        | Thr           | ÷                     |          |
| Phe<br>225 | Thr        | Asp        | Ala        |            |            |             |            |           | Asn        |           |            |            |            |            | Ile<br>240    |                       |          |
| Arg        | Ile        | Ile        | Lys        |            |            |             |            |           |            |           |            |            |            |            |               | . 4                   |          |
| Thr        | Asn        | Leu        | Arg<br>260 | Lys        | Lys        | Glu         |            |           | Lys        |           | Çi ç. i    |            |            |            | Cys           | te di                 |          |
| Leu        | Arg        | Gly<br>275 | Met        | Asn        | Leu        | Ala         | Ser<br>280 | Phe       | Phe        | Ser       | Ala        | Ser<br>285 | Lys        | Ile        | Ile           |                       |          |
| Val        | Phe<br>290 | Val        | Thr        | Phe        | Thr        | Thr<br>295  | Tyr        | Val       | Leu        | Leu       | Gly<br>300 | Ser        | Val        |            | Thr           | 167.                  |          |
| Ala<br>305 | Ser        | Arg        | Val        | Phe        |            |             |            |           |            |           |            |            |            |            |               |                       |          |

| Thr        | 'Val              | Thr        | Len        | Phe<br>325 | Phe        | Pro        | Ser        | Ala        | 11e<br>330 | Glu        | Arg         | Val        | Ser        | Glu<br>335 | Ala        |
|------------|-------------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------|------------|------------|------------|------------|
| Ile        | Val               | Ser        | 11e<br>340 | Arg        | Arg        | Ile        | Gln        | Thr<br>345 | Phe        | Leu        | Leu         | Leu        | Asp<br>350 | Glu        | Ile        |
| Ser        | Gln               | Arg<br>355 | Asn        | Arg        | Gln        | Leu        | Pro<br>360 | Ser        | Asp        | Gly        | Lys         | Lys<br>365 | Met        | Val        | His        |
| Val        | Gln<br>370        | Asp        | Phe        | Thr        | Ala        | Phe 375    | Trp        | Asp        | Lys        | Ala        | Ser<br>380  | Glu        | Thr        | Pro        | Thr        |
| Leu<br>385 | Gln               | Gly        | Leu        | Ser        | Phe<br>390 | Thr        | Val        | Arg        | Pro        | Gly<br>395 | Glu         | Leu        | Leu        | Ala        | Val<br>400 |
| Val        | Gly               | Pro        | Val        | Gly<br>405 | Ala        | Gly        | Lys        | Ser        | Ser<br>410 | Leu        | Leu         | Ser        | Ala        | Val<br>415 | Leu        |
| Gly        | Glu               | Leu        | Ala<br>420 | Pro        | Ser        | His        | Gly        | Leu<br>425 | Val        | Ser        | Val         | His        | Gly<br>430 | Arg        | Ile        |
| Ala        | Tyr               | Val<br>435 | Ser        | Gln        | Gln        | Pro        | Trp<br>440 | Val        | Phe        | Ser        | Gly         | Thr<br>445 | Leu        | Arg        | Ser        |
| Asn        | Ile<br>450        | Leu        | Phe        | Gly        | Lys        | Lys<br>455 | Tyr        | Glu        | Lys        | Glu        | Arg<br>460  | Tyr        | Glu        | Lys        | Val        |
| Ile<br>465 | Lys               | Ala        | Cys        | Ala        | Leu<br>470 | Lys        | Lys        | Asp        | Leu        | Gln<br>475 | Leu         | Leu        | Glu        | Asp        | Gly<br>480 |
| Asp        | Leu               | Thr        | Val        | Ile<br>485 | Gly        | Asp        | Arg        | Gly        | Thr<br>490 | Thr        | Leu         | Ser        | Gly        | Gly<br>495 | Gln        |
| Lys        | Ala               | Arg        | Val<br>500 | Asn        | Leu        | Ala        | Arg        | Ala<br>505 | Val        | Tyr        | Gln         | Asp        | Ala<br>510 | Asp        | Ile        |
| Tyr        | Leu               | Leu<br>515 | Asp        | Asp        | Pro        | Leu        | Ser<br>520 | Ala        | Val        | Asp        | Ala         | Glu<br>525 | Val        | Ser        | Arg        |
| His        | <b>Leu</b><br>530 | Phe        | Glu        | Leu        | Суз        | Ile<br>535 | Cys        | Gln        | Ile        | Leu        | His<br>540  | Glu        | Lys        | Ile        | Thr        |
| Ile<br>545 | Leu               | Val        | Thr        | His        | Gln<br>550 |            | Gln        | -          |            | 555        |             |            |            | Gln        | Ile<br>560 |
| Leu        | Ile               | Leu        | Lys        | Asp<br>565 | Gly        | ГÀЗ        |            |            | 570        | Lys        | Gly         | Thr        |            | Thr<br>575 |            |
| Phe        | Leu               | Ŀуs<br>·   | Ser<br>580 |            | Ile        |            | Phe        | Gly<br>585 | Ser        | Leu        | Leu         | Lys        | Lys<br>590 | Asp        | Asn        |
| Glu        | Glu               | Ser<br>595 | Glu        | Gln        |            | Pro        | Val<br>600 | Pro        | Gly        | Thr        | Pro         | Thr<br>605 | Leu        | Arg        |            |
| Arg        | Thr<br>610        | Phe        | Ser        |            |            |            |            |            | Ser        | Gln        | Gln:<br>620 | Ser        |            | Arg        | Pro        |

| Ser<br>625 | Leu        | ГÀЗ        | Asp        | Gly        | Ala<br>630 | Leu        | Glu        | Ser                 | Gln           | Asp<br>635 | Thr               | Glu        | Asn               |            | Pro<br>640   |                   |
|------------|------------|------------|------------|------------|------------|------------|------------|---------------------|---------------|------------|-------------------|------------|-------------------|------------|--------------|-------------------|
| Val        | Thr        | Leu        | Ser        | Glu<br>645 | Glu        | Asn        | Arg        | Ser                 | Glu<br>650    | Gly        | Lys               | Val        | Gly               | Phe<br>655 | Gln          |                   |
| Ala        | Tyr        | Lys        | Asn<br>660 | Tyr,       | Phe        | Arg        | Ala        | Gly<br>665          | Ala           | His        | Trp               | Ile        | Val<br>670        | Phe        | Ile          |                   |
| Phe        | Leu        | Ile<br>675 | Leu        | Leu        | Asn        | Thr        | Ala<br>680 |                     | Gln           | Val        | Ala               | Tyr<br>685 | Val               | Leu        | Gln          |                   |
| Asp        | Trp<br>690 | _          | Leu        | Ser        | Tyr        | Trp<br>695 | Ala        | Asn<br>Juli<br>Juli | . J           | Gln        | Ser<br>700        | Met<br>nef | Leu<br>Det<br>Tea |            | Val          | ,                 |
| Thr<br>705 | Val        | Asn        | Gly        | Gly        | Gly<br>710 | Asn        | Val        | Thr                 | Glu           | Lys<br>715 | Leu               | Asp        | Leu               | Asn        | Trp<br>720   | ,                 |
| Tyr        | Leu        | Gly        | Ile        | Tyr<br>725 | Ser        | t. J. 8    | Leu<br>,   | Thr                 | Val<br>730    | Ala        | <b>Thr</b><br>948 | Val        | Leu               | Phe<br>735 | Gly          |                   |
| Ile        | Ala        | Arg        | Ser<br>740 | Leu        | Leu        | Val        | Phe        | Tyr<br>745          | Val           | Leu        | Val               | Asn        | Ser<br>750        | Ser        | Gln          | •                 |
| Thr        | Leu        | His<br>755 | Asn        | Lys        | Met        | Phe        | Glu<br>760 | Ser                 | Ile<br>) & pi | Leu        | Lys               | Ala<br>765 | Pro               | Va1        | Leu          | •                 |
| Phe        | Phe<br>770 |            | Arg        | Asn        | Pro        | 11e<br>775 | Gly        | Arg                 | Ile           | Leu        | Asn<br>780        | Arg        | Phe               | Ser        | Lys          | ٠,                |
| Asp<br>785 | Ile        | G1y        | His        | Leu        | Asp<br>790 | Asp        | Leu        | Leu                 | Pro           | Leu<br>795 | Thr               | Phe        | Leu               | Asp        | Phe<br>800   |                   |
| Ile        | Gln        | Thr        | Leu        | Leu<br>805 | Gln        | Val        | Val        | Gly                 | Val<br>810    | Val        | Ser               | Val        | Ala               | Val<br>815 | Ala          |                   |
| Val        | Ile        | Pro        | Trp<br>820 | Ile        | Ala        | Ile        | Pro        | Leu<br>825          | Val           | Pro        | Leu               | Gly<br>:   | Ile<br>830        | Ile        | Phe          |                   |
| Ile        | Phe        | Leu<br>835 | Arg        | Arg        | Tyr<br>X   | Phe        | Leu<br>840 | Glu                 | Thr           | Ser        | Arg               |            | Val               | Lys        | Arg          |                   |
| Leu        | Glu<br>850 | Ser        |            | Thr        |            |            |            |                     |               |            |                   |            | Ser               | Ser        | Ser          |                   |
| Leu<br>865 | Gln        | Gly        | Leu        | Trp        | 870        | Ile        | Arg        | Ala                 | Tyr           | 875        | Ala               | Glu<br>/   | Glu               | Arg        | Cys<br>- 880 |                   |
| Gln        | Glu        | Leu        | Phe        | Asp<br>885 | Ala        | His        | Gln        | Asp                 | Leu<br>890:   | His        | Ser<br>v orti     | Glu        | Ala               | Trp<br>895 | Phe          | ·                 |
| L u        | Phe        | Leu        | Thr<br>900 | Thr        | Ser        | Arg        | 235        | Phe<br>905          | Ala           | Val        | Arg               | ζ          | Asp<br>910        | Ala        | Ile          | ्रक छ<br>इस्त्राच |
| Суз        | Ala        |            |            | Val        |            |            |            | 1 1 3               |               |            |                   |            | 1 75              |            |              |                   |
| Lys        | Thr        | Leu        | Asp        | Ala        | Gly        | Gln        | Val        | Gly                 | Leu           | Ala        | Leu               | Ser        | Tyr               | Ala        | Leu          |                   |

|             | 930         |             |             |             | ď           | 935          |             |             | 1           |             | 940         |             |             |             |             |
|-------------|-------------|-------------|-------------|-------------|-------------|--------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|
| Thr<br>945  | Leu         | Met         | Gly         | Met '       | Phe<br>950  | Gln          | Trp         | Cys         |             | Arg<br>955  | Gln         | Ser         | Ala         | Glu         | Val<br>960  |
| Glu         | Asn         | Met         | Met         | Ile<br>965  | Ser         | Val          | Glu         | Arg         | Val<br>970  | Ile         | Glu         | Tyr         | Thr         | Asp<br>975  | Leu         |
| Glu         | Lys         | Glu         | Ala<br>980  | Pro         | Trp         | <b>Glu</b> ∘ | Tyr         | Gln<br>985  | Lys         | Arg         | Pro         | Pro         | Pro<br>990  | Ala         | Trp         |
| Pro         | His         | Glu<br>995  | Gly         | Val         | Ile         | Ile          | Phe<br>1000 |             | Asn         | Val         | Asn         | Phe<br>1005 | Met         | Tyr         | Ser         |
| Pro         | Gly<br>1010 |             | Pro         | Leu         | Val         | Leu<br>1015  |             | His         | Leu         | Thr         | Ala<br>1020 | Leu<br>)    | Ile         | Lys         | Ser         |
| Gln<br>1025 |             | Lys         | Val         | Gly         | Ile<br>1030 |              | Gly         | Arg         | Thr         | Gly<br>1035 | Ala         | Сlу         | ГЛЗ         | Ser         | Ser<br>1040 |
| Leu         | Ile         | Ser         | Ala         | Leu<br>1045 |             | Arg          | Leu         | Ser         | Glu<br>1050 | Pro         | Glu         | Gly         | Lys         | Ile<br>1055 | Trp         |
| Ile         | Asp         | Lys         | Ile<br>1060 |             | Thr         | Thr          | Glu         | Ile<br>1065 | Gly         | Leu         | His<br>. ^. | Asp         | Leu<br>1070 | Arg<br>)    | Lys         |
| Lys         | Met         | Ser<br>1075 |             | Ile         | Pro         | Gln          | Glu<br>1080 |             | Val         | Leu         | Phe         | Thr<br>1085 |             | Thr         | Met         |
| Arg         | Lys<br>1090 |             | Leu         | Asp         | Pro         | Phe<br>1095  |             | Glu         | His         | Thr         | Asp<br>1100 | Glu<br>)    | Glu         | Leu         | Trp         |
| Asn<br>1105 |             | Leu         | Gln         | Glu         |             | Gln<br>) ; . |             | ГÀЗ         | Glu         | Thr<br>1115 | Ile         | Glu         | Asp         | Leu         | Pro<br>1120 |
| Gly         | Lys         | Met         | Asp         | Thr<br>1125 |             | Leu          | Ala         | Glu         | Ser<br>1130 |             | Ser         | Asn         | Phe         | Ser<br>113  | <b>Val</b>  |
| Gly         | Gln         | Arg         | Gln<br>1140 |             | Val         | Суз          | Leu         | Ala<br>114  |             | Ala         | Ile         | Leu         | Arg<br>115  | Lys<br>0    | Asn         |
| Gln         | Ile         | Leu<br>115  |             | Ile         | Asp         | Glu          | 1160        | Thr<br>)    |             | Asn         |             | Asp<br>116  | 5           | Arg         | Thr         |
| Asp         | Glu<br>1170 |             | Ile         | Gln         | Lys         | Lys<br>117   | Ile         |             |             | Lys         |             | Ala         |             | Суз         | Thr         |
| Val<br>118  |             | Thr         | Ile         | Ala         | His<br>119  |              | Leu         | Asn         | Thr         | Ile<br>119  |             | Asp         | Ser         | Asp         | Lys<br>1200 |
| Ile         | Met         | Val         | Leu         | Asp<br>120  |             | Gly          | Arg         | Leu         | Lys<br>121  |             | Tyr         | Asp         | Glu         | Pro<br>121  | Tyr<br>5    |
| <b>V</b> al | Leu         | Leu         | Gln<br>122  |             | ГЛЗ         | Glu          | Ser         | Leu<br>122  |             | Tyr         | Lys         | Met         | Val<br>123  | Gln<br>O    | Gln         |
| Leu         | Gly         | Lys         |             | Glu         | Ala         | Ala          | Ala         |             | Thr         | Glu         | Thr         | Ala<br>124  | Lys<br>5    | Gln         | Arg         |

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<210> 553
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Ser Ile Cys Asn Met Thr Cys Ala Ser Val Phe Phe Cys Asp Gln Lys
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            Val Leu Asn Ser Gln Ala Thr Asp Ser Tyr Gln Ser Thr Asp Tyr Tyr
           Glu Pro His His Thr Gly Gly Glu His
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Leu Gln Lys Asn Lys Leu Arg Ala Ser Thr Asp Ser Thr Leu Trp Ile
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                                                                                              the second section in the second
 Cys Ala Ala Glu Ala Ser Thr Lys Pro Tyr Phe Tyr Thr Cys Leu Val
                                     ာ များကြဲ 20 (နှို့ <sub>မြန်မျိ</sub>း ကြိုနှိုင်းကြို 25) ကြိမ်းမြန်းကျပ် ရပ်မျိုး ၅၂<mark>30</mark> များကြိုမ်းမြန်းကျပြန်း မြန်မျိုး
မေးများ မြန်မျိုး မြန်မျိုးများ ရန္တော်များများ မြန်မျိုးများများ မြန်မျိုးများများ မြန်မျိုးများများ ကျွန်မေးများ
 Met Leu His Gly Gln Gly Leu Ala Leu Leu Ser Pro Thr Asn Leu Pro
                                     🚁 35 m.a. Hrans Propalito a shiritati na Habitati na Propalito Propalitori na Pr
                                      . ಚಲಿಸುವ ಸಂಪರ್ಕತೆಗೊಂಡಲಾಗಿ ಸುತ್ತಿಗಳ ಪ್ರಕ್ರೀಯ ಕನ್ನಡುವ ಸಂಗ್ರಹಿಸುವ ಸಂಪರ್ಕತೆಗಳು ಸಂಪರ್ಕತೆಗಳು ಕುಮ್ಮಾನಿಕರು ಕುಮ್ಮಾನಿಕರು
 Glu Ile Leu Arg Phe Leu Phe Asn Gly Phe Leu State San Cast August a man a
                            50 Mg ^{\circ} Hg, the highest 55 Gg, fit is such a subdigible. The \zeta is the \zeta dimension of subset fit yes
                                                                ခရာကေရာက္သည့္ကို သင္တေနရည္အခ်ိန္တာကို အစ္တရားမွာ နည္းလည္း မွည္ေတြသည့္သည္ လည္းသည္ကို ရာသည္ကို မွာျပည္သည္သည္။
                                        Anna the same in a committee of the comm
 <212> PRT
                                                            riging and the contract of the d can be a substituted in a property of the contract of the c
  <213> Homo sapiens and a latter way in it was a distribution of the contract o
                                Homo sapiens எது இடம்கள் இது இரு இருக்கு இருக்கு இருக்கு இது இது இது இது இது இருக்கு இருக்கு இது இருக்கு இது இ
இந்த இருக்கு இருக்கு இது இருக்கு இது இது இருக்கு இது இருக்கு இருக்கு இருக்கு இருக்கு இருக்கு இருக்கு இருக்கு இ
555 இருக்கு இர
  <400> 555 | Length of the property and c
 Leu Gly Arg Phe Ser Leu Ser Cys Lys Ser Gly His Ser Arg Gly Gln
                            ່ວ່າ ກໍຄົວເຂົ້າ ຄົວເຂົ້າ ຄົວເຕ
                                                                                                                                                                                                                                                        and my
 Pro Gln Leu Gly Ala Thr Ala Gln Gly Lys Val His Met Gly Leu Ser
                                  134 1
 Thr Ala Gln Gly Ser Ile Gln Asp Ile Lys Val Pro His Ser Ile Asp
                                 35 ... 40 ... 45 ... 45 ...
Leu Val Ala Lys Lys Lys Gln Thr Leu Ile Ser Phe Cys His Pro
                            50 (4) 21 (4) (4) (55) (4) (4) (4)
                                                                                                                                                                                     The Committee of the Co
 Ser Asp Pro Leu Glu Leu Leu
<210> 556
 <211> 81
 <212> PRT
  <213> Homo sapiens
                                                                     ాళ్ళ కుముకుడ్ని విధిక కూడు.
మా
Asn His Pro Glu Gln Gly Ser Ser Thr Pro Arg Pro Gln Thr His Thr
                                                                           _{2} , _{3} , _{5} , _{5} , _{6} , _{7} , _{6} , _{7} , _{7} , _{7} , _{7} , _{7} , _{7} , _{7}
Ser Pro Arg Thr Ile Met Asn His Thr Thr Gln Glu Glu Val Ser Thr
                                                                     20 | 1 | 19 | 1 | 1 | 1 | 1 | 1 | 25 | 25 | 25 | 19 | 1 | 26 | 19 | 1 | 1 | 30 | 30 | 30 | 1 | 27 | 1 | 40 |
Arg Gln Ala Lys Glu Ala Ser Pro Val Leu Thr Ala Thr Arg His Gly
                                                                                                                                                                                                          is a about a £ 45 km iy ka horonask nik boroni.
Ser Tyr Tyr Ser Leu Asn Ser Ala Ser Thr Gln Ile Ser Asp Asn Ile
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50 55 60 Arg Asn Ser Leu Glu His Glu Pro Cys Cys Glu Leu Pro Ile Arg Arg 75 7.0 Ile <210> 557 <211> 54 <212> PRT <213> Homo sapiens Ser Leu Ser Ala Thr Pro Leu Thr Leu Trp Asn Ser Ser Asp Pro Leu 1 10 Glu Gln Ala Tyr Leu Ile Ser Ala Arg Glu Lys Thr Asn Asn Gly Leu 25 20 30 Lys Gly Ser Leu Thr Met Lys Val Ser Ala Asn Ser Trp Leu Arg Cys 40 45 Gly Phe His Ile Arg Phe , 50 1. 13. 1. 1. 1. 1. <210> 558 <211> 77 <212> PRT <213> Homo sapiens <220> <221> VARIANT <222> (1)...(77) <223> Xaa = Any amino acid <400> 558 Asn Asp Arg Asp Arg Asn Ser Asn Lys Val Ile Xaa Lys Ala Asn Leu Ile Tyr Phe Thr Asn Leu Thr Ser Cys Leu Ser Val Gln Asn Gln Thr 30 20 25 Phe Thr Cys Thr Lys Arg His Lys His Leu Gln Cys Ser Ser Val His 45. Leu Cys Lys Ile Pro Pro Arg Leu Lys Gly Arg Asp Lys Lys Lys **55** Pro Ser Tyr Leu Ser Gly Val Leu His Ser Arg Ser Tyr 75 **70** <210> 559 15 1 m 1 2 " <211> 50

<212> PRT

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Thr Asn Pro Val Val' Asn Cys Leu Ser Glu Gly Ser Arg Leu Cys Ala
Ser Tyr Glu Asn Leu Met Pro Asp Asp Leu Ser Leu Ser His Phe Ala
                           40
Pro Arg
                                  ्रिक्षी वस्त्र अवैद्ये सम्बद्धे १५६८ ५०%।
<210> 560
<211> 56
                               THE HER DAY THE WAS
<212> PRT
<213> Homo sapiens
           BUT GAR GOVERNMENT A DE BOOK LOOK
<400> 560
Ile Gly Ser Leu Lys Gly Pro Thr Thr Ala Gly Ser His Cys Ser Gly
                                                15
                                  10
Glu Gly Ser Tyr Gly Thr Phe Tyr Cys Pro Arg Phe Tyr Thr Gly Tyr
Lys Gly Ala Ser Gln Tyr Arg Ser Gly Ser Lys Glu Glu Glu Thr Asn
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           BAR SERVICE SERVICE A PROPERTY OF THE SERVICE
<400> 561
Val Leu His Leu Asp Gln Met Asn Asn Val Gly Ile Xaa Met Asp Lys
           Gly Leu Lys Ser Pro Glu Ile Lys Asn Pro Ala Pro Thr Gly Thr Ser
                      25
보고 하는 10 등에 다시 회복 교육 12개 등의 128 등 1
Asn Leu Ser Cys Phe Leu Ser Xaa Phe Trp Leu Met Gln Gly Thr Asn
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Ser Leu Pro Arg Glu Asn Tyr Leu Asn

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Ala Pro Met His Gly Ile Lys Asn Ser Ile Thr Ser Leu Ile Phe Leu
                                                 25 30
Ile Ser Tyr Leu Xaa Leu Glu Met Ser Ser Leu Ser Glu Ser Leu Val
                  35 40 45 45
Leu Ser Ser Gly Asp Tyr Val Leu Asp Thr Pro
            55 55
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Cys Phe Leu Phe Pro Tyr Leu Trp Leu Tyr Ala Gln Pro Leu Phe Pro
Lys Gln Gln Pro Pro Ala Leu Ala Pro Gly His Pro Asp Phe Ile His
Thr Gln Asn Glu Gln Ile Asp Pro Ser Pro His Ile Gln Asn Leu Met
                      35 The second of \mathbf{40} , \mathbf{40}
Trp Asn Pro His Leu Ser Gln Glu Leu Ala Glu Thr Phe Met Val Arg
           Asp Pro Leu Arg Pro Leu Leu Val Phe Ser Leu Ala Asp Ile Arg
          - 1970年 - 70日 - 1987年 - 1987年 - 1987年 - 1987年 - 1984年 - 1987年 - 19
<210> 564
                                                                                                                        大块。1900年1月1日 1800年1月1日 1801日 1801
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Val Arg His Leu Tyr Ile Leu Tyr Arg Thr Leu Gly Ser Arg Lys Ser 40 His Met Asn Leu Pro Leu Ser Ser Gly Ser Gln Leu Trp Leu Ala Pro 60 50 55 <210> 565 <211> 57 <212> PRT <213> Homo sapiens Try The rich Car St. <221> VARIANT <222> (1)...(57) <223> Xaa = Any amino acid Leu Tyr Tyr Cys Ser Tyr Leu Cys His Phe Arg Thr Ala Leu Ile Leu 5 10 A GARAGE TO SERVE Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln 25 . 30 20 Asn Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu 35 40 45 1994 St 2 . . . 1 Tyr Ala Val Ser Ser Xaa His Asn Val <210> 566 <211> 55 <212> PRT <213> Homo sapiens Control of the Contro

Ile Leu Leu Glu Phe Phe Arg Asn Gln Arg Gly Ser Leu Asn Pro Arg 

Lys Thr Val Pro Phe Ile Lys Ser Glu Gly Gly Glu Lys Lys Gly His 

Cys Asn His Ser Val Val Ser Ile Asp Ser Ala Ala Ala Leu Leu Pro

Leu Lys Leu Val Leu Leu Pro

<210> 567 <211> 51

<212> PRT

<213> Homo sapiens

Tyr Ser Asp Phe Asp Val Phe Cys Ser His Thr Tyr Gly Tyr Met Leu

The state of the s

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|-------------------|-------------------------|-------------------|--------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|------------------|-------------------------|------------|------------------|--------------|-----------------|---------------------|----------------|-----------------------------------------------|----------------------------------------------|------------------------------------------------------|-------------|
| <2:<br><2:<br><2: | l0> 5<br>l1> 1<br>l2> 2 | 573<br>L32        | • .          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                          | 5.7 t            | 4 24.75<br>4 4          | ,          |                  | rair<br>Orto | •               | i kari<br>Malayan   | da.eg<br>.akta | ر و مث<br>ا                                   | Hite San |                                                      |             |
|                   | 00> 5                   |                   | sapı         | ens                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                          |                  |                         |            | ı                |              |                 |                     |                |                                               | •                                            | 1.13                                                 |             |
|                   |                         |                   | Gly          | Glu<br>5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Gly<br>,                 | Glu<br>,         | Ala                     | Arg        | His<br>10        | Vål          | Leu             | His                 | 'Gly           | Gly<br>15                                     | Arg                                          | 5 (d.<br>1911)<br>1913 - 1913                        |             |
| Arg               | g Glu                   | الأوارد 🚅         | - 20         | 1:5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 15, 3                    | (S)              | Thr i                   | 25         | 100              | e , s        |                 | يوالمرازية          | - 30           |                                               | والمناجيرين                                  |                                                      |             |
| Glr               |                         | Ser               | Gly          | Pro                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Val                      | Ala              | Gln                     | Ala        | Gly              | Val          | Gln             | Trp                 | His            | Asp                                           | Leu                                          | en de<br>En en designi<br>En engleuri.<br>En edirent | 14 1.       |
| Ser               | Ser                     | Leu               | Gln          | Pro                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Leu                      | Pro              | His A                   | out<br>Ara | Phe              | Lvs          | Gln             | e la<br>Phe         | Ser            | . or n<br>-Cvs.                               | Ten.                                         | < ************************************               | <br>        |
| Ser               | Leu                     | Pro               | His          | Ser                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Trp                      | Asp              | His 1                   | ::<br>Arg  | Tyr              | Ala          | Pro             | Pro                 | His            | Leu                                           | Ala                                          | /                                                    |             |
| 65                |                         | 16.5<br>1943      | - 2. j       | 3 25 g<br>5 5 5 5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | · ±70                    | 1 # 1 m          | , 55                    |            | a sidi.<br>Ta    | 75           | ដូ <u>សិ</u> ្  | 49.                 |                | J 1                                           | 80,                                          |                                                      | : ··. ·     |
|                   |                         | 44 · · ·<br>⇒∷    | acht<br>La b | း <b>စည</b> ့်<br>ျင်းသ                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | (4)                      | inings<br>Sabib  | Najvičija<br>Silonomija |            | . 90.            | uru *        | ook S<br>gele   | ound:<br>Sand       | k              | - 95                                          | idalək<br>H                                  | (1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -             | F**         |
|                   |                         | - 111             | 100          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | ₹ .                      | * (15 B). (      | . 9 ,1                  | LQ5        |                  | - * *        | (, <u>;;</u> ); | 1000                | 110            | ار ته د. ـ                                    | مفرية بالمها                                 | ngger -                                              | 17 C        |
| ГЛS               | Cys                     | Trp<br>115        | Gly          | Tyr                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Arg                      | His              | Lys I<br>120            | Pro        | Pro              | His          | Pro             | Ala<br>125          | Суз            | His                                           | Ile                                          |                                                      |             |
| Leu               | Leu<br>130              | Asn               | Tyr          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                          | 1                |                         |            |                  |              |                 |                     |                | •                                             | ি হৈ                                         |                                                      |             |
| <21               | 0> 5°                   | / Table 1         |              | . "7" 2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                          |                  | 1.1                     |            | . ,              | _            |                 | 4 44                |                | A 4 1 4 1 4 1 1 1                             |                                              |                                                      | ~,          |
| <21:<br><21:      | 1> 6.<br>2> PI<br>3> Ho | z<br>RTj<br>omo s | sapie        | ens                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | rg i<br>Gradi<br>Histori |                  | ili<br>ur               | j,         |                  | · .          |                 | ili.<br>Vediv<br>Cd |                | ,<br>,<br>, , , , , , , , , , , , , , , , , , | i i i i i i i i i i i i i i i i i i i        |                                                      |             |
| <40               | 0> 51                   | 74                | aug.<br>Iaud | ಗಳನ್ನು.<br>ಕಾಕಕೂತ                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | id di.<br>Yil ger        | * 5 300<br>- 800 | 53 (* )<br>5 (* )       | åe<br>∵i   | Arq              |              | ۲.              | 3.2°                | • :            | 7. ±                                          | Asn                                          |                                                      |             |
|                   |                         | organisa<br>Togan | . e ç. ; ;   | : ; <b>5</b> -:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | ng di<br>Graft           | aşər<br>Hədi     | er (d)<br>Silving       | •••        | 10               | har.         | · · · ·         | ·                   | 7.2            | 15                                            |                                              |                                                      | 1,<br>· · - |
| • .               |                         | 100 e<br>130 c    | 20           | i de la composition della comp |                          | 1 907.<br>5 1    | ក្នុងប្រ<br>ការប្រ      | 25         | i india<br>Notae |              |                 | t přist.            | 30             | وغوا<br>وغوال                                 |                                              |                                                      | :           |
| GIA               | Arg                     | Thr<br>35         | Ser          | Glu '                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Gly :                    | Gly 1            | Asp C<br>40             | ys 🚶       | His              | Lys          | Lęu             | Phe<br>45           | Phe            | Phe (                                         | Glu                                          | * 2 . 4 · ·                                          |             |
| Thr               | Arg<br>50               | Val               | Trp          | Pro (                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Cys (                    | Cys I<br>55      | Pro G                   | ly :       | Trp              | Ser :        | Ala<br>60       | Val .               | Ala            |                                               | and the second                               | 20%<br>30%                                           | ;<br>,      |
| <210              | > 57                    | 5                 |              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                          |                  |                         |            |                  |              |                 |                     |                | .i.                                           | at any mak                                   | តាលផងិ<br>ពេល                                        | ,           |

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 Ser Leu Glu Pro Gly Arg Leu Arg Glu Glu Asn Arg Leu Asn Pro Gly
                                                                                        40
 Gly Arg Gly Cys Ser Glu Pro Arg Ser Cys Cys Cys Thr Pro Ala Trp
                50 55 60
 Ser Thr Glu Gln Asp Ser Ala Ser Lys Thr Asn Lys
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 <221> VARIANT
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 <223> Xaa = Any Amino Acid
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 Arg Gln Ala Pro Gly Asn Trp Lys Met Xaa Ser Lys Cys His Ala Gln
  Leu Leu Phe Thr Phe Tyr Leu Asn His Phe Tyr Gln Ile Arg Leu Asn
                                                                                                                                           60
  Pro Gly Tyr Ser
                                                                                                                                                                                                             185 J.M.
  <210> 577
  <211> 57
  <212> PRT
                                                                                                                                                                                   A STATE STATE OF
  <213> Homo sapiens
                                                                  CONTRACTOR OF SECTION OF A SECT
  <400> 577
  Met Tyr Leu Glu Asn Ser Phe Tyr Cys Gln Met Ile Leu Leu Lys Arg
```

Cys Arg Leu Ser Lys Ile Ser Thr Gln Arg Val Val Pro Asp Gly Pro

20 30 25 'Pro Ala Pro Val Pro Gly Ser Phe Pro Met Phe Pro Arg Phe Gly Phe 40 Arg Leu Ala Pro Pro Ala Asp Thr Pro Section of the second <210> 578 <211> 51 <213> Homo sapiens ా కు 41. ఈ కాటకు ఉన్నారి అన్నాయి. ఈ సినిముకు మాట్లుకు కాటికి కు <400> 578 Met Gln Leu Ile Tyr Leu Cys Phe Leu Gly Leu Leu Tyr Ile Arg His His Asp Ser Gln Ser Phe Val Ile Leu Tyr Tyr Lys Lys Leu Asn Tyr Tyr Phe Lys Tyr Gly Gln Ile Arg Ala Phe His Ile Ala Lys Val Tyr 40 Gln Pro His 50 (83, 1. (1) AL. <210> 579 bisi omina was - tus <211> 56 <212> PRT <213> Homo sapiens <400> 579 Met His Phe Thr Phe Met Gln Leu Ile Tyr Leu Cys Phe Leu Gly Leu Leu Tyr Ile Arg His His Asp Ser Gln Ser Phe Val Ile Leu Tyr Tyr 20 25 Lys Lys Leu Asn Tyr Tyr Phe Lys Tyr Gly Gln Ile Arg Ala Phe His 35 4 40 7 Ile Ala Lys Val Tyr Gln Pro His 50 <210> 580 <211> 67 <212> PRT <213> Homo sapiens 8.000 000 000 0 <400> 580 <400> 580
Met Glu Leu Arg Thr Lys Ala Leu Arg Thr Ala Gln Gln Leu Thr Ser ୍ରୀର ୧**୭**୧ ତିଲ୍ଲିର ୧୯ ୧୯ ୧୯ ଅଟେ ଅ<mark>ଟି ମେନ୍ତି ହେନ୍ତି କଥାଚିତ୍ର 15</mark>ର ମ Cys Val Thr Ala Leu Lys Ala Ala Gly Pro Pro L u Thr Phe Trp Lys

20 1. June 14 100 (25/17) A 464 10 1 10 6 30 1 1 1 1

Phe Ile His 65

<210> 581 <211> 77 <212> PRT <213> Homo sapiens

and suppose

<400> 581
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Ala His Ile Leu Glu Gly Lys Met Gly Thr Met Leu Ser Ala Thr Leu 50 55 60

Gly Pro Ser Trp Val Thr Cys Ile Leu His Leu Cys Ser 65 70 75

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20 25 30.

Lys Leu Cys Leu Glu Phe Leu Cys Gly Val Trp Phe Gly Leu Gly Phe
35 40 45

Leu Gly Val

<210> 583 <211> 60 <212> PRT <213> Homo sapiens

<400> 583

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<210> 586 <211> 60 <212> PRT <213> Homo sapiens

Leu Phe 50

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Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu Ala Ser Leu Gly Ser Ser
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Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu Leu Phe
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agecegeeg gtgaageteg etgettteee taceteetta agtgaetgee aaaegeeeae 120
cggctggaat tgctctggtt atgatgacag agaaaatgat ctcttcctct gtgacaccaa 180
cacctgtaaa tttgatgggg aatgtttaag aattggagac actgtgactt gcgtctgtca 240
gttcaagtgc aacaatgact atgtgcctgt gtgtggctcc aatggggaga gctaccagaa 300
tgagtgttac ctgcgacagg ctgcatgcaa acagcagagt gagatacttg tggtgtcaga 360
aggatcatgt gccacagatg caggatcagg atctggagat ggagtccatg aaggctctgg 420
agaaactagt caaaaggaga catccacctg tgatatttgc cagtttggtg cagaatgtga 480
cgaagatgcc gaggatgtct ggtgtgtgtg taatattgac tgttctcaaa ccaacttcaa 540
teceetetge gettetgatg ggaaatetta tgataatgea tgeeaaatea aagaageate 600
gtgtcagaaa caggagaaaa ttgaagtcat gtctttgggt cgatgtcaag ataacacaac 660
tacaactact aagtetgaag atgggeatta tgeaagaaca gattatgeag agaatgetaa 720
caaattagaa gaaagtgcca gagaacacca cataccttgt ccggaacatt acaatggctt 780
ctgcatgcat gggaagtgtg agcattctat caatatgcag gagccatctt gcaggtgtga 840
tgctggttat actggacaac actgtgaaaa aaaggactac agtgttctat acgttgttcc 900
eggteetgta egattteagt atgtettaat egeagetgtg attggaacaa tteagattge 960
tgtcatctgt gtggtggtcc tctgcatcac aaggaaatgc cccagaagca acagaattca 1020
cagacagaag caaaatacag ggcactacag ttcagacaat acaacaagag cgtccacgag 1080
gttaatctaa agggagcatg tttcacagtg gctggactac cgagagcttg gactacacaa 1140
tacagtatta tagacaaaag aataagacaa gagatotaca catgttgcct tgcatttgtg 1200
gtaatctaca ccaatgaaaa catgtactac agctatattt gattatgtat ggatatattt 1260
gaaatagtat acattgtctt gatgtttttt ctgtaatgta aataaactat ttatatcaca 1320 .
caatawagtt ttttctttcc catgtatttg ttatatataa taaatactca gtgatgagaa 1380
aaaaaaaaa aaaaaaaaaa rwmqaccc
<210> 588
<211> 81
<212> PRT
<213> Homo sapiens
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Met Pro Gln Lys Gln Gln Asn Ser Gln Thr Glu Ala Lys Tyr Arg Ala
                                     10
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Leu Gln Phe Arg Gln Tyr Asn Lys Ser Val His Glu Val Asn Leu Lys 20 25 30

```
Gly Ala Cys Phe Thr Val Ala Gly Leu Pro Arg Ala Trp Thr Thr Gln
 Tyr Ser Ile Ile Asp Lys Arg Ile Arg Gln Glu Ile Tyr Thr Cys Cys
 Leu Ala Phe Val Val Ile Tyr Thr Asn Glu Asn Met Tyr Tyr Ser Tyr
                                                                80
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Met Thr Met Cys Leu Cys Val Ala Pro Met Gly Arg Ala Thr Arg Met
Ser Val Thr Cys Asp Arg Leu His Ala Asn Ser Arg Val Arg Tyr Leu 20 25 30
Trp Cys Gln Lys Asp His Val Pro Gln Met Gln Asp Gln Asp Leu Glu
35 40
Met Glu Ser Met Lys Ala Leu Glu Lys Leu Val Lys Arg Arg His Pro
Pro Val Ile Phe Ala Ser Leu Val Gin Asn Val Thr Lys Met Pro Arg
65 70 75 80
Met Ser Gly Val Cys Val Ile Leu Thr Val Leu Lys Pro Thr Ser Ile 85 90 95
Pro Ser Ala Leu Leu Met Gly Asn Leu Met Ile Met His Ala Lys Ser
100 105 110
Lys Lys His Arg Val Arg Asn Arg Arg Lys Leu Lys Ser Cys Leu Trp
115
120
125
Val Asp Val Lys Ile Thr Gln Leu Gln Leu Leu Ser Leu Lys Met Gly
130
140
Ile Met Gln Glu Gln Ile Met Gln Arg Met Leu Thr Asn
<210> 590
                                                             1952902 . . . . .
<211> 347
<212> PRT
<213> Homo sapiens to the challe man and out als we also all the same
<400> 590
Met Leu Leu Ile Val Ala Arg Pro Val Lys Leu Ala Ala Phe Pro Thr
```

|            |            |            |            |            |            |            |            |            |            |               | •          |            |            |            |            |   |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|---------------|------------|------------|------------|------------|------------|---|
| Ser        | Leu        | Ser        | Asp<br>20  | Cys        | Gln        | Thr        | Pro        | Thr<br>25  | Gly        | Trp           | Asn        | Суз        | Ser<br>30  | Gly        | Tyr        |   |
| Asp        | Asp        | Arg<br>35  | Glu        | Asn        | Asp        | Leu        | Phe<br>40  | Leu        | Cys        | Asp           | Thr        | Asn<br>45  | Thr        | Cys        | Lys        |   |
| Phe        | Asp<br>50  | Gly        | Glu        | Суѕ        | Leu        | Arg<br>55  | Ile        | Gly        | Asp        | Thr           | Val<br>60  | Thr        | Суз        | Val        | Суз        |   |
| Gln<br>65  | Phe        | Lys        | Cys        | Asn        | Asn<br>70  | Asp        | Tyr        | Val        | Pro        | <b>Val</b> 75 | Cys        | GLY        | Ser        | Asn        | Gly<br>80  |   |
| Glu        | Ser        | Tyr        | Gln        | Asn<br>85  | Glu        | Суз        | Tyr        | Leu        | Arg<br>90  | Gln           | Ala        | Ala        | Cys        | Lys<br>95  | Gl'n       |   |
| Gln        | Ser        | Glu        | Ile<br>100 | Leu        | Val        | Val        | Ser        | Glu<br>105 | Gly        | Ser           | Суз        | Ala        | Thr<br>110 | Asp        | Ala        |   |
| Gly        | Ser        | Gly<br>115 | Ser        | Gly        | Asp        | Gly        | Val<br>120 | His        | Glu        | Gly           | Sēr        | Gly<br>125 | Glu        | Thr        | Ser        |   |
| Gln        | Lys<br>130 |            | Thr        | Ser        | Thr        | Cys<br>135 | Asp        | Ile        | Суз        | Gln           | Phe<br>140 | Gly        | Ala        | Glu        | Cys        |   |
| Asp<br>145 | Glu        | Asp        | Ala        | Glu        | Asp<br>150 | Val        | Trp        | Cys        | Val        | Cys<br>155    | Asn        | Ile        | Asp        | Cys        | Ser<br>160 |   |
| Gln        | Thr        | Asn        | Phe        | Asn<br>165 |            | Leu        | Суз        | Ala        | Ser<br>170 | Asp           | Gly        | Lys        | Ser        | Tyr<br>175 | Asp        |   |
| Asn        | Ala        | Суз        | Gln<br>180 |            | Lys        | Glu        | Ala        | Ser<br>185 | Суз        | Gln           | Lys        | Gln        | Glu<br>190 | Lys        | Ile        |   |
| Glu        | Val        | Met<br>195 |            | Leu        | Glý        | Arg        | Cys<br>200 | Gln        | .Asp       | Asn           | Thr        | Thr<br>205 | Thr        | Thr        | Thr        |   |
| Lys        | Ser<br>210 |            | Asp        | Gly        | His        | Tyr<br>215 | Ala        | Arg        | Thr        | Asp           | Tyr<br>220 | Ala        | Glu        | Asn        | Ala        | , |
| 225        | _          |            |            |            | 230        |            |            |            |            | 235           |            |            | •          | į.         | Glu<br>240 |   |
| His        | Tyr        | : Asn      | Gly        | Phe 245    | Cys        |            | His        |            | Lys<br>250 | Cys           | Glu        | His        | Ser        | 255        | Asn        |   |
| Met        | Gln        | Glu        | 260        |            | Cys        | Arg        | Cys        | Asp<br>265 |            | Gl.y          | Tyr        | Thr        | G13<br>270 | Glr        | His        |   |
| Cys        | Glu        | Lys<br>275 |            |            | Туг        |            | Val<br>280 |            | Туг        | . Val         | Val        | Pro<br>285 | Gly        | , Pro      | Val        |   |
| Arg        | Phe<br>290 |            | Tyr        | · Val      | Leu        | 11e<br>295 |            | Ala        | Val        | Ile           | 300        |            | : Ile      | Glr        | lle        |   |
| Ala<br>305 |            | Ile        | e Cys      | : Val      | Val<br>310 |            | Leu        | Cys        | : Ile      | Thr<br>315    |            | Lys        | в Су:      | e Pro      | Arg<br>320 |   |

```
Ser Asn Arg Ile His Arg Gln Lys Gln Asn Thr Gly His Tyr Ser Ser
                                                          325 ... 330<sub>19 (1996</sub> ...
  Asp Asn Thr Thr Arg Ala Ser Thr Arg Leu Ile
                                            340
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  <211> 565
  <212> DNA
  <213> Homo sapien
  <400> 591
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  aaacagacaa aaaatattgt acaacattgc acccagtgtc agattctaca cctgccact
                                                                                                                                                                                                                                                          180
 caggaagcaa gagttaatcc cagaggtcta tgtcctaatg tgttatggca aatggatgtc atgcacgtac cttcatttgg aaaattgtca tttgtccatg tgacagttga tacttattca catttcatat gggcaacctg ccagacagga gaaagtactt cccatgttaa aagacatta
                                                                                                                                                                                                                                                         300
                                                                                                                                                                                                                                                          360
  ttatcttgtt ttcctgtcat gggagttcca gaaaaagtta aaacagacaa tgggccaggt
                                                                                                                                                                                                                                                         420
 tactgtagta aagcatttca aaaattctta aatcagtgga aaattacaca tacaatagga
                                                                                                                                                                                                                                                          480
  attototata attoccaagg acaggocata attgaaggaa ctaatagaac actcaaagct
                                                                                                                                                                                                                                                         540
  caattggtta aacaaaaaaa aaaaa
                                                                                                                                                                                                                                                         565
 <210> 592
                                               with the constraint u=0 by f(u)=0 for f(u)=0 for f(u)=0
 <211> 188
  <212> PRT
 <213> Homo sapien
                                                                    The second of the particle of 
 <400> 592
 Thr Lys Ala Asn Glu Gln Ala Asp Leu Leu Val Ser Ser Ala Phe Ile
1 5 10 15
 Glu Ala Gln Glu Leu His Ala Leu Thr His Val Asn Ala Ile Gly Leu
                                                                                                          ...25
 Lys Asn Lys Phe Asp Ile Thr Trp Lys Gln Thr Lys Asn Ile Val Gln
 His Cys Thr Gln Cys Gln Ile Leu His Leu Ala Thr Gln Glu Ala Arg
                               55
 Val Asn Pro Arg Gly Leu Cys Pro Asn Val Leu Trp Gln Met Asp Val
65 70 75 80 Met His Val Pro Ser Phe Gly Lys Leu Ser Phe Val His Val Thr Val
Asp Thr Tyr Ser His Phe Ile Trp Ala Thr Cys Gln Thr Gly Glu Ser 100 105 110
 Thr Ser His Val Lys Arg His Leu Leu Ser Cys Phe Pro Val Met Gly
115 120 125
Val Pro Glu Lys Val Lys Thr Asp Asn Gly Pro Gly Tyr Cys Ser Lys
                                                                                 135
Ala Phe Gln Lys Phe Leu Asn Gln Trp Lys Ile Thr His Thr Ile Gly
145
150
150
160
Ile Leu Tyr Asn Ser Gln Gly Gln Ala Ile Ile Glu Gly Thr Asn Arg
165
Thr Leu Lys Ala Gln Leu Val Lys Gln Lys Lys Lys Lys 175
180
185
                                                 A AND MADERIC THE MAD MAD MAD THE RAME TO $ 2000 A TO 1000 A AND A CONTRACTOR AND A CONTRAC
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vi :

BNSDOCID: <WO\_\_\_0151633A2\_I\_>

<210> 593

<211> 271

```
<212> DNA
<213> Homo sapien
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tgtgcnccca nagcaacctg ggcacgcggg gacagggggg ccnacaattg agggagcggt
gteectaget ggggtetata catgnenggg naagggenge tgagtneeat nagcaaagga
nctagnatnt gcgggggtgc ggcctgggcc taccctttna agcatccntn gatccactcc
angaanceng gggtagneag gtttnecaac a
<210> 594
<211> 376
<212> DNA
<213> Homo sapien
<220>
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cetttggggg nggggggaac etttaceatt gincecettt atticatitg gitngggite
                                                                        60
gegeeetenn gggeeaacaa agttategin nitgaagaga anattititt ggntingnee
                                                                       120
cgattaagcg ncaaatgtgt agcaaaangc cgtgccactt gtggcgtagc tncgtcgggt
                                                                       180
cgattcgacg acaaggcgtn gcgcgntanc gttagtctcn aatngacccn gtggcatgag
                                                                       240
eccaegangg nttegtgteg teacatggne tetagacata aegeneneen ttttttneag
                                                                       300
agggggntgc cgcccttagg gaggnagggg tggggacact agccaancca nantctnacc
                                                                       360
                                                                       376
ccattgaaga aaaggn
<210> 595
<211> 242
<212> DNA
<213> Homo sapien
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<221> misc_feature
<222> (1)...(242)
<223> n = A, T, C or G
<400> 595
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tgngnatgcc aggcaaggnc aagctggctc aaaaagcatc cacccacctc tgnaangggt
atgccangag cangigcacc agtcccaact angagnecen ggcatgntac atcttcttcc
accectnaaa ntttgngeta caangneeat ttttetttt etettaaggg nenentgget
                                                                       240
<210> 596
<211> 535
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
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```
<222> (1) ... (535)
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     <400> 596
     accagttgga tactgctaaa nagatattta tgcagcctca tatgttaagt cgtatatttt
                                                                                                                                                                                                                                                                                                                           60
     gaaagetttt taaatttttt etttaagaag attttagatg ettateaetg agtaceagag
                                                                                                                                                                                                                                                                                                                      120
    ggatgtagge tgatgccett atcaacaaag tcagggactg tggcacacaa ggattgacta
                                                                                                                                                                                                                                                                                                                      180
     ctgcagacac ggccacaatg ctacctctag agggcctgaa tccccctgcc ctctctggtg
                                                                                                                                                                                                                                                                                                                      240
     gggagaaggg ctggcagagc cattagcatg ggctccggcc aatcctggcc actttgacac
                                                                                                                                                                                                                                                                                                                       300
    tcctggtgct gacccagggt cctggaggaa gggatgaggt gggcagtaga gatgctcagg
     gcagtggccc ctttccatcc acactggaac tatttcagta ttttaccacc aattcagcca
    ttcccttgtg cgctggctga acatcagccc tgctccaggt ctcagtttcc cctttgtaaa
                                                                                                                                                                                                                                                                                                                      480 🐇
    gggaaagctc tggattcagg gagtgatgaa gaggtcatca tggtcttgag aattc
                                                                                                                                                                                                    ମଧିକିଥିଲେ ଅଟିଆରୀ ଅଧ୍ୟକ୍ତ ହେଉଛି । ୧୯୯
୨୭୫୫ ଓଡ଼ିଆ ବିଅନ୍ତ ଓଡ଼ିଆ ଓଡ଼ିଆ ନୁଦ୍ର ଅ
    <210> 597
    <211> 257
    <212> DNA
    <213> Homo sapien
                                                                                                                                                                                                                                                                                                     . 12. 175
                                                                                                                                                                                                                                                                            1 July 19 18 87 87 5
    <220>
    <221> misc_feature
    <222> (1) ... (257)
                                                                                                                                                                                                                                                                              2-32-33-5-53
    <223> n = A, T, C or G
    <400> 597
    tttcnatacc caaaantacc ccatattang accanacatt tgtctnggaa aaattaccat
    tntntaacnt ttgggccacc tgagannaaa tgggtgtaat ncatgataag atggancagn
   attrictetta agatringatri agaccegtt titeaeggaa catateeaag nacceaatag gnaacaagee aegggnggag teacaaacat atateetta eteteataat cegtrineaea 240 naactritign aettgae 257
   naactnttgn acttgac
                                                                                                                                                                            ing the growded regulation in the Samuel State of Samuel S
                                                                                                               in each on agency on portarionally gyreque.
    <210> 598
                                                                                                               5. e ::
                                                                                                                                                                          Committee of the contraction of 
    <211> 222
                                                                                                                                                                                                                                                                    300 13 B B 15
    <212> DNA
    <213> Homo sapien
    <220>
    <221> misc feature
    <222> (1)...(222)
    <223> n = A,T,C or G
    <400> 598
   nntggntacc gtcnaaactt nncttggtac ccgagctcgg atccactagt ccagtgtggt:
   ggaattccat tgtgttgggc tataagctgt aatagtggag ncgtgctngg ttcattgcan
                                                                                                                                                                                                                                                                                                                      120
   nagnecetee geanneache ttgnnacaae etgtgagnag genataaatt atteacataa
                                                                                                                                                                                                                                                                                                                     180
   tcatcactgc atgaanctga ctcaaacgca tccacntaca cc
                                                                                                                                                                                                                                                                                                                     222
                                                  നു പ്രകാരത്തെ അവരുമാന് വരുന്നു. നിന്നു വരുന്നു വിന്നു വരുന്നു വരു വരുന്നു വരു വരുന്നു.
ഇത്രസ്ത്രം പ്രവര്ത്തെ വരുന്നു അവരുന്നു ആവരുന്നു പ്രത്യാത്രം പ്രത്യാത്രം വരുന്നു. വരുന്നു വരുന്നു വരുന്നു വരുന്
 <210> 599
                                                and the control of the complete of the control of t
<211> 238
                                                      in the first of a constitue for an estate for the discount above is severe in the constituency of the
   <212> DNA
   <213> Homo sapien
                                                                                                                                                                                                                                                                                                         ~; -- .(
   <220>
   <221> misc_feature
   <222> (1)...(238)
   <223> n = A,T,C or G
   <400> 599
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```
qcatqacatc ancqatqtnt ttggnnacct ganattngct aaaactngng natgccgggn
atgnaggttt ggtantgate tatgcaetea cateteatgg ggaegtttea tgtggagtgn
                                                                      120
tcgacaangt tgctgnancn gagaagtgat gatctcagtt gaaagggtca tgtgaataca
                                                                      180
cnttacactt gaaaaagaag cacattggga atatcacgaa acgnecacca acatectg
                                                                      238
<210> 600
<211> 232
<212> DNA
<213> Homo sapien
<220>
<221> misc_feature
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<223> n = A,T,C or G
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tactcatcag agctaaatga gagcgcttta aaaatgttag tttgtcttcc gccatttcta
                                                                      120
                                                                      180
cagaaagctg caatttcagg ttttcaacct aataggtgat atttaanaaa aaaaaaaagc
aatcgcaaat agccccactg cttttacaaa tcatttttc cccaacacaa tg
<210> 601
<211> 547
<212> DNA
<213> Homo sapien
<221> misc_feature
<222> (1)...(547)
<223> n = A, T, C \text{ or } G
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tttttcttaa atatcaccta ttaggttgaa aacctgaaat tgcagctttc tgtagaaatg
                                                                      120
gcggaagaca aactaacatt tttaaagcgc tctcatttag ctctgatgag tactacaccc
                                                                      180
ctnatattct tctgatacta aaataatttt cctagtgtag tctaaacttt tttaaaaaga
                                                                      240
                                                                      300
catgtaatcc gcggagttag taactcaaaa cgagtgcatc tnggaagtat cgcagccgtt
nctggatnaa attcccagct tgctngcttg ctnagccggg gggcggtnaa aaaaacatct
                                                                      360
gcagccongg ggnaaaaacc ttcgcattgt tcttacgtgt ttacgttatt ttatttccct
                                                                      420
nnagcaaggc nggganttgg ggactcgaaa tggtacagtt gggctgggga tcgcccttgt
                                                                      480
                                                                  540
tacataaaag ncgtccagaa gagggacggt tacaggcngg ganctccaaa ggtcagtccc
                                                                      547
tgccatt
<210> 602
                                                         and the second
<211> 826
<212> DNA
<213> Homo sapien
                 a dalam kacamatan teori baga ya kebinda jiya sustab dibaray takta i maƙarata b
<221> misc_feature <222> (1)...(826)
<223> n = A,T,C or G
<400>,602
cggggggnnt tacgtctctc tggacgcttt tattgtacca gggcgatccc agcccaactg
taccattcga gtccctactc ctgccttgct ctagggaaat aaaataacgt aaacacgtaa 120
gaacaatgcg aaagcgtttt cttccctagg ctgcagattg tcttcttcac cgcccctgct 180 tagctagcta gctagctggg aatttaatcc agaaacggct tgcgatacct cctagatgca 240
```

of part of with the first

222

```
ctcgttttga gttacaaact ccgcggatta catgtctttt taaaaaagtt tagactacac
                                                                      300
tagggaaaat tattttagta tcagaagaat atcagggggt gtagtactca tcagagctna
                                                                      360
atgagagege titaaaaatg ttagtttgte tteegeeatt tetacagaaa getgeaattt
                                                                       420
                                                                      480
caggttttca ncctaatagg tgatatntaa gaaaaaaaaa acaatcgcan atagcccact
gettttacaa atcatttttc tettetaggt atageetgte aggtggeeta atgtattttt
                                                                      540
gacatctcta ggaattttaa tagaccagaa atgggtgcca gagatatgcc tgcactaatc
                                                                       600
ttaagtgggg atttatgtat ttctcaanca agtgattaaa gcaaaactag gcacgaatga
                                                                       660
aatcaagatc tttaggccag aaatcatgaa nanttttana attatttan gaatctgtgg
                                                                      720
                                                                      780
cttctcttct taaaatngaa aaaaaattg tttaaaccca naaggtctga atacccaagc
                                                                      826
nccctgaacn anagaacaan gccggagcac cccctcccaa atcccc
                                                           eri Bolling P
<210> 603
                                                         Carty The Sol
<211> 817
<212> DNA
<213> Homo sapien
                No. in a control of the second section is the coupy second asset to be un-
<220>
<221> misc_feature
<222> (1)...(817)
<223> n = A,T,C or G
<400> 603
                                                                    * * 60° ±
nnangacttt tgtqqtntta tacaattntt ttttctattt ctatgaagag aaagccacag
                                                                      120
agtectaaaa taattetaaa acteateatg actttettge etaaaagate ttgattteaa
tcgtgcctag ttttgcttta atcacttgct tgagaaatac ataaatcccc acttaagatt
                                                                      180
agtgcaggca tatctctggc acccatttct ggttctatta aaattcctag agatgtcaaa
                                                                      240
aattacatta ggccacctga caggctatac ctagaagaga aaaaatgatt tgtaaaagca
                                                                      300
qtqqqqctat ttqcqattqc ttttttttt tcttaaatat cacctattag gttgaaaacc
                                                                      360
                                                                      420
tgaaattgca gctttctgta gaaatggcgg aagacaaact aacattttta aagcgctctc
atttagetet gatgagtaet acaccetga tattettetg atactaaaat aatttteeta 480
gtgtagtcta aacttttta aaaagacatg taatccgcgg agtttgtaac tcaaaacgag
                                                                      540
tgcatctagg aggtatcgca agccgtttct ggattaaatt cccagctagc ttgcttgctt
                                                                      600
agcagggcg ggnaaanaag acatctgcag cctagggaag aaaacctttc gcattgttct
                                                                      660
tacqtqttta cqttatttta tttcctanaa caaggcngaa ttgggactcg aatggttcag
ttggggtggg ggatcccctg gtncataaaa ngtcanaaag anggtacagg cggaacncca
                                                                       780
agggtcgtcc tgcatttana ctcggaattt tggtgcc

<210> 604

<211> 694

<212> DNA

<213> Homo sapien
                                                                      817
<220>
<221> misc feature
<222> (1)...(694)
<223> n = A,T,C or G
<400> 604
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gacateteta ngaattttaa tagaaccaga aatgggtgee agagatatge etgeactaat 💮 🤲 120
cttaagtggg gatttatgta tttctcaagc aagtgattaa agcaaaacta ggcacgattg - 1180
aaatcaagat cttttaggca anaaagtcat gatgagtttt agaattattt taggactctg 240
tggctttctc ttcatagaaa tagaaaaaaa aattgtataa aaccacaaaa ggtcctgaat
agccaaagca acactganca aaaagaacan agcagggaag caacacacta congaattca
aattatacta ccagggtgta gtaaccaaaa cagcattcta ttggcataaa atagacacca 4 420
agaccaatgg ancagaataa agaaccccac aaataaatce atatatatatatac cgccanctga 480
ttatcaataa cnaacaccaa gaacatatht taagggacht-nctattcaat aantagtget 500 540 600
ggnaaaaact gggaaatcca tatgcagaaa naatgaaact agacccctat ccctcaccat
```

```
acqcaaannt caacttegga atgggattac aaaacttaag acattecaac ecaagaaact
                                                                       660
atnaaancta ctattaagaa aacagatcnc nccc
                                                                       694
<210> 605
<211> 678
<212> DNA
<213> Homo sapien
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<221> misc_feature
<222> (1)...(678)
<223> n = A, T, C or G
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                                                                       120
agaaagctgc aatttcaggt tttcaaccta 'ataggtgata tttaagaaaa aaaaaaagca
                                                                       180
ategeaaata geeceactge ttttacaaat catttttet ettetaggta tageetgtea
                                                                       240
ggtggcctaa tgtaattttt gacatctcta ggaattttaa tagaaccaga aatgggtgcc
                                                                       300
agagatatgc ctgcactaat cttaagtggg gatttatgta tttctcaagc aagtgattaa
                                                                       360
agcaaaacta ggcacgattg aaatcaanat cttttaggca agaaagtcat gatgagtttt
                                                                       420
anaattattt taggactetg tggetttete tteatagaaa tagaaaaaaa aaattgtata
                                                                       480
aaaaccacaa aaggteetga atageecaaa geaacaetga acaaaangaa caaageagga
                                                                       540 -
agcaacacac taccggaatt caattatact accaaggtgt antaaccaaa acagcattct
                                                                       600
attgggcata aaatagacca aagaccagtg ggaaacagaa taaagaancc caaaataaat
                                                                       660
cctatattta cngcccnc
                                                                        678
<210> 606
<211> 263
<212> DNA
<213> Homo sapien
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<221> misc_feature
<222> (1)...(263)
<223> n = A, T, C or G
<400> 606
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totagtocae tgtgntcaaa ttecattgtg tgggggcene tegeetegge canagatetg
                                                                      120
agtgancana entgteecea etgaggtgee ceacagengn ttgtntteag cangggetna
                                                                       180
caactegace ggcagegnan ggctggcaga antgngcgcc tnnctcatte ctacgengtn
                                                                       240
ngccgcagga aggangacag gcc
                                                                       263
<210> 607
<211> 22
<212> DNA
<213> Artificial Sequence
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<223> Primer
<400> 607
                                                                        22
ccatgtgggt cccggttgtc tt
<210> 608
<211> 22
<212> DNA
```

| <213>          | Artificial  | l Seguenc               | :e              |                                       |                                                                                                                                                                                                                                 |                   |                                             |                                            |
|----------------|-------------|-------------------------|-----------------|---------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|---------------------------------------------|--------------------------------------------|
| 1220           |             |                         |                 |                                       |                                                                                                                                                                                                                                 |                   | P. 2                                        | es a la l |
| <220>          |             | '                       | ,               |                                       |                                                                                                                                                                                                                                 |                   |                                             |                                            |
| <223>          | Primer      |                         |                 |                                       |                                                                                                                                                                                                                                 |                   |                                             | 1.70                                       |
|                |             | t ,                     |                 |                                       |                                                                                                                                                                                                                                 |                   | •                                           |                                            |
| <400>          |             | 1.                      |                 |                                       |                                                                                                                                                                                                                                 |                   |                                             |                                            |
| gatage         | gggtg ctca  | ggggtt gg               | Ī               |                                       |                                                                                                                                                                                                                                 |                   | . '                                         | 22                                         |
| -010>          | 600         |                         | •               |                                       | *                                                                                                                                                                                                                               |                   |                                             |                                            |
| <210><br><211> |             | *                       | •               | 1                                     |                                                                                                                                                                                                                                 |                   |                                             |                                            |
| <211>          |             |                         |                 |                                       | 1                                                                                                                                                                                                                               |                   |                                             |                                            |
|                | Artificia:  | Seguenc                 | :e              |                                       |                                                                                                                                                                                                                                 |                   |                                             |                                            |
|                |             |                         |                 |                                       |                                                                                                                                                                                                                                 |                   |                                             |                                            |
| <220>          |             | . '_                    |                 |                                       |                                                                                                                                                                                                                                 |                   |                                             | ,                                          |
| <223>          | Brimer      | dagan <sup>i</sup> , en | والمناه والمناه |                                       |                                                                                                                                                                                                                                 | <u>.</u> .        | SM. 12 70                                   | 2 2 <sup>4</sup> 11275                     |
|                |             | વિકાર્યો છે.            | 2 J. W. L.      | 10g 100 作品E                           | udd 201,                                                                                                                                                                                                                        | <b>ಸ್ಕಾ</b> ರ್ಥಿಕ | ្តាស្ត្រី នគរ 🙉                             | rija etsektitak                            |
| <400>          | 609 Spag    | . :                     | 26.2 ៖ ដូរ៉ូត   | Brandy Ar                             | r <sub>at</sub> door is:                                                                                                                                                                                                        | Bod.              |                                             |                                            |
| gctgga         | acagg gggc  | aaaagc tg               | gggcagtg        | aaccatgtg                             | 📮 (dažila i sp.                                                                                                                                                                                                                 |                   |                                             | 40                                         |
| 201Ax          | 610         | a Jing s                | 12.75           | 8.7795 (A.)                           | y in 1994, 2021<br>The Common State of the Common                                                                                               |                   | i Production (                              |                                            |
| -              |             |                         |                 |                                       |                                                                                                                                                                                                                                 |                   |                                             | and the sire                               |
| <2117<br><2117 | DNA         |                         | n tiga kan ka   |                                       | radio de la deservación de la decembración de la decembración de la decembración de la decembración de la dec<br>La decembración de la decembración | • / - ;           | gillerin kun ett i<br>Otta en ott tillerini | Constant of                                |
| <213>          | Artificia.  | l Segueno               | :e              | and Lab                               |                                                                                                                                                                                                                                 |                   |                                             | 5                                          |
| 10.00          |             | - 0,5 4                 |                 | · · · · · · · · · · · · · · · · · · · |                                                                                                                                                                                                                                 |                   |                                             | A. 5.1                                     |
| <220>          | 2           |                         |                 |                                       |                                                                                                                                                                                                                                 |                   |                                             |                                            |
| <223>          | Primer      |                         |                 |                                       |                                                                                                                                                                                                                                 |                   |                                             |                                            |
|                | •           |                         | •               | ٠                                     |                                                                                                                                                                                                                                 |                   |                                             |                                            |
| <400>          |             | ,                       |                 |                                       |                                                                                                                                                                                                                                 |                   |                                             | 0.77                                       |
| ccttgt         | ccag atago  | cccagt ag               | ıctgac          |                                       |                                                                                                                                                                                                                                 |                   |                                             | 27                                         |
| <210>          | 611         |                         |                 |                                       |                                                                                                                                                                                                                                 |                   |                                             |                                            |
| <211>          |             |                         |                 |                                       |                                                                                                                                                                                                                                 |                   | ٠.                                          | •                                          |
| <212>          |             |                         |                 |                                       |                                                                                                                                                                                                                                 |                   |                                             |                                            |
| <213>          | Artificial  | l Sequenc               | :e'             |                                       |                                                                                                                                                                                                                                 |                   |                                             |                                            |
|                | •           | -                       | t               |                                       |                                                                                                                                                                                                                                 |                   |                                             | ,                                          |
| <220>          |             |                         |                 |                                       |                                                                                                                                                                                                                                 |                   |                                             |                                            |
| <223>          | Primer      |                         |                 |                                       |                                                                                                                                                                                                                                 |                   |                                             |                                            |
| 44005          | C11         |                         |                 |                                       | •                                                                                                                                                                                                                               |                   |                                             |                                            |
| <400>          |             |                         |                 |                                       |                                                                                                                                                                                                                                 |                   |                                             | 46                                         |
| gataga         | agaaa accgi | cecagg ec               | aguacege        | gggaggctg                             | y gagtge                                                                                                                                                                                                                        |                   |                                             | 40                                         |
| <210>          | 612         | va in T                 |                 |                                       |                                                                                                                                                                                                                                 |                   | •                                           |                                            |
| <211>          |             |                         |                 |                                       | • 1: *                                                                                                                                                                                                                          |                   | •                                           |                                            |
| <212>          |             |                         |                 |                                       |                                                                                                                                                                                                                                 |                   |                                             |                                            |
| <213>          | Artificial  | L Sequenc               | e               |                                       |                                                                                                                                                                                                                                 |                   |                                             |                                            |
|                |             |                         |                 | •                                     |                                                                                                                                                                                                                                 |                   |                                             |                                            |
| <220>          |             |                         |                 |                                       |                                                                                                                                                                                                                                 |                   |                                             | •                                          |
| <223>          | Primer      |                         |                 | 5                                     |                                                                                                                                                                                                                                 | . 1               | · . :                                       | •                                          |
| Z4005          | 612         |                         |                 |                                       |                                                                                                                                                                                                                                 |                   |                                             |                                            |
| <400>          |             | 100002 00               | tttaaaa         | cctgtccag                             | •                                                                                                                                                                                                                               |                   |                                             | 40                                         |
| gcaval         | -yyıl Gacıç | jecejca yo              | LLLLYUUU        | Julyludage                            | -                                                                                                                                                                                                                               |                   |                                             | 40.                                        |
| <210>          | 613         |                         |                 |                                       |                                                                                                                                                                                                                                 |                   |                                             |                                            |
| <211>          |             |                         |                 |                                       |                                                                                                                                                                                                                                 | ::                |                                             | and the arms of the                        |
| <212>          |             | •                       |                 |                                       |                                                                                                                                                                                                                                 |                   | * *                                         |                                            |
|                | Artificial  | Sequenc                 | e               |                                       |                                                                                                                                                                                                                                 |                   |                                             | *** .                                      |
|                |             |                         |                 |                                       |                                                                                                                                                                                                                                 |                   |                                             |                                            |
| ~22N\          |             |                         |                 |                                       |                                                                                                                                                                                                                                 |                   |                                             |                                            |

| <223> Prime: | r           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              |                          |                                       |
|--------------|-------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|------------------------------|--------------------------|---------------------------------------|
| :            | _           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              |                          | 10 S                                  |
| <400> 613    |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              |                          | 2 <b>(</b>                            |
| gccgctcgag   | ttagaattcg  | gggttggcca                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | castaata     | 1                            |                          | 38                                    |
| geogerogus   | coagaaccog  | 9990099000                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | -94-55-5     |                              |                          |                                       |
| <210> 614    | ı           | 27%                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |              |                              |                          | 3 . *                                 |
| <211> 53     |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | , ,,         | •                            |                          |                                       |
| . –          | •           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              | 144 121                  | 1 10 1                                |
| <212> DNA    |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              |                          |                                       |
| <213> Artif  | iciai seque | ence                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |              |                              | , *,                     | 4.4                                   |
|              |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              |                          |                                       |
| <220>        | 4           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 1            |                              |                          | ~ 1                                   |
| <223> Prime: | r           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              |                          |                                       |
|              |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              |                          | · · · · · · · · · · · · · · · · · · · |
| <400> 614    |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              | •                            |                          |                                       |
| cggcgggcat   | atgcatcacc  | atcaccatca.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | catcataaac   | ggcgaggact                   | gca                      | <b>53</b> ·                           |
|              |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              | and the second of the second | -                        |                                       |
| <210> 615    | _           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | **           | 1                            |                          |                                       |
| <211> 46     |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              |                          |                                       |
| <212> DNA    |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              |                          |                                       |
| <213> Artif. | icial Seque | ence                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |              | · ·                          |                          | , ,                                   |
| 1            |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              |                          |                                       |
| <220>        |             | 5 " .                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |              |                              |                          |                                       |
| <223> Prime: | *           | 4 £                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |              |                              |                          |                                       |
| \223> EIIMG  | -           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              | · 14 .                   | 1. 1. 1. 1.                           |
| 4400x C1E    |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              | 1                        |                                       |
| <400> 615    |             | مأعم ما المام الما | ~~~~         | tatata                       | A Commence of the second | 46                                    |
| gcactcccag   | cctcccacaa  | tactggcctg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | gaeggtttte   | ECLATC                       | 2 -                      | 40                                    |
|              | **:         | 19 1 18 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 1 1          | gradient de Agrico           |                          |                                       |
| <210> 616    | •           | ÇÎL                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | **           |                              |                          |                                       |
| <211> 1350   | 137 D       | er ger                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |              |                              |                          |                                       |
| <212> DNA    |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | •            | •                            |                          |                                       |
| <213> Homo   | sapien      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              | • .                      | •                                     |
|              |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              |                          |                                       |
| <400> 616    |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              |                          |                                       |
| atgcatcacc   | atcaccatca  | catcataaac                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | ggcgaggact   | gcagcccgca                   | ctcgcagccc               | 60 -                                  |
| tggcaggcgg   | cactggtcat  | ggaaaacgaa                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | ttgttctgct   | cgggcgtcct                   | ggtgcatccg               | 120                                   |
| cagtgggtgc   |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              |                          | 180                                   |
| cacagtettg   |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              |                          | 240                                   |
| cggcacccag   |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              |                          | 300                                   |
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|              |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              | aatgcctacc               | 420                                   |
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| ggaaaagccc   |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              |                          | 720                                   |
| actgagtgga   |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              |                          |                                       |
| cattcccaac   |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              |                          | 780                                   |
| ctggtgcacc · | cccagtgggt  | cctcacagct                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | gcccactgca   | tcaggaacaa                   | aagcgtgatc               | 840                                   |
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| cacagettee   | cacacccgct  | ctacgatatg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | agcctcctga   | agaatcgatt                   | cctcaggcca               | 960                                   |
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| gatgctgtga : | aggtcatgga  | cctgcccacc                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | caggagccag   | cactggggac                   | cacctgctac               | 1080                                  |
| gcctcaggct   | ggggcagcat  | tgaaccagag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | gagttcttga   | ccccaaagaa                   | acttcagtgt               | 1140                                  |
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| aagttcatgc   |             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |              |                              |                          | 1260                                  |
| gccctgcccg   | 22222222    | cctatacaca                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | aadataataa   | attaccoras                   | atagatasa                | 1320                                  |
| goodly order | tagagagaga  | constitutes                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | -agg cgg cgc | -coursey, gaa                | guggacodag               | 1350                                  |
| gacaccatcg ' | Lygocaacço  | cyaattotda                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | • }          |                              |                          | 1000                                  |

<210> 617

<211> 449

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355 Pro Glu Glu Phe Leu Thr Pro Lys Lys Leu Gln Cys Val Asp Leu His ່ 375 ຶ່ Val Ile Ser Asn Asp Val Cys Ala Gln Val His Pro Gln Lys Val Thr 395 385
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|   | ctootcaaaa                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | ggaaccaaga                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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|   | gctgggctca<br>agccagtgaa<br>cacatcaatg<br>atccacaatg<br>agcggaaact<br>agatatttgg<br>cggatcttct<br>atccttcgct<br>catcttgtga<br>ggatcgtttc<br>gaagtcttca<br>agatctccag<br>tttgaaaaaa<br>gcatgcccat<br>agaggaagct<br>ttcacagact                                                                                                                                                                                                                                                   | gtttagatta<br>acatattect<br>tettagaact<br>aacacaagtg<br>tgatgatage<br>getgeetegg<br>tttttggt<br>ttggtttegg<br>aaagggaaag<br>ttggtateta<br>ttteeetgtg<br>geaetttaat<br>ggagaactag<br>etgeaeagtg<br>gtaaageact<br>tgatteate                                                                                                                                                                                                                                                                                                                         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|   | gctgggctca<br>agccagtgaa<br>cacatcaatg<br>atccacaatg<br>agcggaaact<br>agatatttgg<br>cggatcttct<br>atccttcgct<br>catcttgtga<br>ggatcgtttc<br>gaagtcttca<br>agatctccag<br>ttgaaaaaa<br>gcatgccat<br>agaggaagct<br>ttcacagact<br>tgcttaaaac                                                                                                                                                                                                                                       | gtttagatta<br>acatattect<br>tettagaact<br>aacacaagtg<br>tgatgatage<br>getgeetegg<br>ttttttgtgt<br>ttggtttegg<br>aaagggaaag<br>ttggtateta<br>ttteeetgtg<br>geaetttaat<br>ggagaactag<br>etgeaeagtg<br>gtaaageaet<br>tgaatteate<br>ttgagaaaca                                                                                                                                                                                                                                                                                                        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|   | gctgggctca<br>agccagtgaa<br>cacatcaatg<br>atccacaatg<br>agcggaaact<br>agatatttgg<br>cggatcttct<br>atcttgtga<br>ggatcgtttc<br>gaagtcttca<br>agatctccag<br>ttgaaaaaa<br>gcatgccat<br>agaggaagct<br>ttcacagact<br>ttgataaaa<br>ctacacaaag                                                                                                                                                                                                                                         | gtttagatta<br>acatattect<br>tettagaact<br>aacacaagtg<br>tgatgatage<br>getgeetegg<br>ttttttgtgt<br>ttggtttegg<br>aaagggaaag<br>ttggtateta<br>ttteeetgtg<br>geaetttaat<br>ggagaactag<br>etgeaeagtg<br>gtaaageaet<br>tgatteate<br>ttgagaaaca<br>atgeaeace                                                                                                                                                                                                                                                                                            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|   | gctgggctca<br>agccagtgaa<br>cacatcaatg<br>atccacaatg<br>atccacaatg<br>agcggaaact<br>agatcttct<br>atccttggt<br>catcttgtga<br>ggatcgtttc<br>gaagtcttca<br>agatctccag<br>tttgaaaaaa<br>gcatgcccat<br>agaggaagct<br>ttcacagact<br>ttcacagact<br>tgctaaaac<br>ctacacaaag<br>gaaagtcaaa                                                                                                                                                                                              | gtttagatta<br>acatattect<br>tettagaact<br>aacacaagtg<br>tgatgatage<br>getgeetegg<br>ttttttgtgt<br>ttggtttegg<br>aaagggaaag<br>ttggtateta<br>ttteeetgtg<br>geactttaat<br>ggagaactag<br>etgeacagtg<br>gtaaageact<br>ttgagaaca<br>atgeacace<br>gtteeeage                                                                                                                                                                                                                                                                                             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|   | getgggetea<br>agecagtgaa<br>cacatcaatg<br>atecacaatg<br>atecacaatg<br>ageggaaact<br>agatettet<br>atectteget<br>catettgtga<br>ggategtte<br>gaagtettea<br>agatetecag<br>tttgaaaaaa<br>geatgeceat<br>agaggaaget<br>tteacagact<br>tteacagact<br>ttgaaaaaa<br>gaaggaaget<br>tteacagact<br>ttgaaaaaa<br>gaaggaaget                                                                                                                                                                   | gtttagatta<br>acatattect<br>tettagaact<br>aacacaagtg<br>tgatgatage<br>getgeetegg<br>ttttttgtgt<br>ttggtttegg<br>aaagggaaag<br>ttggtateta<br>ttteeetgtg<br>geactttaat<br>ggagaactag<br>etgeacagtg<br>gtaaageact<br>ttgagaaca<br>ttgagaaca<br>atgeacatee<br>gtteeeage<br>gacaggeet                                                                                                                                                                                                                                                                  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                                                                                                            | 1300                                                                                                                                         |
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|   | ggaaacttcc                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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                                                                                                            | 1620                                                                                                                                         |
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|   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    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                                                                                                            | 1740                                                                                                                                         |
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|   | <220> <221> misc <222> (1). <223> n = 1 <400> 622                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | feature<br>(3228)<br>A,T,C or G                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                        | 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                              |
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(3228) A,T,C or G                                                                                                                                                                                                                         | ggcggtaggc                                                                                                                                                                                                                                                                                       | gtgtacggtg                                                                                                                                                                                                                                                             | ggaggtctat                                                                                                                                                                                                     | ataagcagag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 60                                                                                                                                           |
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                                                   | feature(3228) A,T,C or G tgacgcaaat aactagagaa                                                                                                                                                                                                      | ggcggtaggc                                                                                                                                                                                                                                                                                       | gtgtacggtg                                                                                                                                                                                                                                                             | ggaggtctat<br>cgaaattaat                                                                                                                                                                                       | ataagcagag<br>acgactcact                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           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                                                             | ataagcagag<br>acgactcact<br>tcggatccac                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 60<br>120<br>180<br>240<br>300<br>360<br>420<br>480<br>540<br>600<br>660<br>720<br>780                                                       |
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(3228) A,T,C or G  tgacgcaaat aactagagaa ccaagctggc tggtggaatt gatgtggagc cactttatcc ttgcccagca aaagaagtct agagttctcc tggtctgatc cctgcttacg atatcagtgg ctctccatac cacgggtgtg                                                              | ggcggtaggc<br>cccactgctt<br>tagcgtttaa<br>ccattgtgtt<br>ccagaggtca<br>cagcacttta<br>gagatcaggt<br>agccacgttt<br>tctgagacct<br>tcagcactcc<br>gggcactctt<br>agagctgcag<br>ggcagccctt                                                                                                               | gtgtacggtg<br>actggcttat<br>acttaagctt<br>gggcaggaaa<br>gggatggctg<br>ggaatactga<br>ccgagagttc<br>gtgtagagcg<br>gatctctgga<br>ttagtctgct<br>agatgcccac<br>caaggtggcc<br>tatttggaaa<br>cttgccctga                                                                       | ggaggtetat cgaaattaat ggtaccgage caagcaaagt tetetetagg ggteatacca cettettaaa getgtgetgt ggetgggeaa cgeefeteee accataaett cetagageea ctteetaaat gageacaegg                                                      | ataagcagag<br>acgactcact<br>tcggatccac<br>ggtggagcag<br>gtccacttgc<br>gccacatett<br>aaaaggagac<br>gctgggggtt<br>tcttgcactt<br>atggcccag<br>ccatgctagt<br>cgcaccagcc<br>cactttgctg<br>gagtgcagca                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 60<br>120<br>180<br>240<br>300<br>360<br>420<br>480<br>540<br>600<br>660<br>720<br>780                                                       |
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                                                   | feature(3228) A,T,C or G  tgacgcaaat aactagagaa ccaagctggc tggtggaatt gatgtggagc cactttatcc ttgcccagca aaagaagtct agagttctcc tggtctgatc cctgcttacg atatcagtgg ctctccatac cacgggtgtg cccacatcaa ttaagcatca                                           | ggcggtaggc<br>cccactgctt<br>tagcgtttaa<br>ccattgtgtt<br>ccagaggtca<br>cagcacttta<br>gagatcaggt<br>agccacgttt<br>tctgagacct<br>tcagcactcc<br>gggcactctt<br>agagctgcag<br>ggcagccett<br>tttgcttta<br>ctgccattaa<br>taagtgaagg                                                                      | gtgtacggtg<br>actggcttat<br>acttaagctt<br>gggcaggaaa<br>gggatggctg<br>ggaatactga<br>ccgagagttc<br>gtgtagagcg<br>gatctctgga<br>ttagtctgci<br>agatgccac<br>caaggtggcc<br>tattggaaa<br>cttgccctga<br>agaaaagaaa                                                           | ggaggtetat cgaaattaat ggtaccgagc caagcaaagt tetetetagg ggtcatacca cettettaaa getgtgetgt ggetgggeaa cgcetetece accataaett cetagageca ctteetaat 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                                                                                                                | 60<br>120<br>180<br>240<br>300<br>360<br>420<br>480<br>540<br>600<br>660<br>720<br>780<br>840<br>900<br>960                                  |
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                                                   | feature(3228) A,T,C or G  tgacgcaaat aactagagaa ccaagctggc tggtggaatt gatgtggagc cactttatcc ttgcccagca aaagaagtct agagttctcc tggtctgatc cctgcttacg atatcagtgg ctctccatac cacgggtgtg cccacatcaa ttaagcatca tttggtatca                                | ggcggtaggc<br>cccactgctt<br>tagcgtttaa<br>ccattgtgtt<br>ccagaggtca<br>cagcacttta<br>gagatcaggt<br>agccacgttt<br>tctgagacct<br>tcagcactcc<br>gggcactctt<br>agagctgcag<br>ggcagcectt<br>ttttgcttta<br>ctgccattaa<br>taagtgaagg<br>ccagatctac                                                       | gtgtacggtg<br>actggcttat<br>acttaagctt<br>gggcaggaaa<br>gggatggctg<br>ggaatactga<br>ccgagagttc<br>gtgtagagcg<br>gatctctgga<br>ttagtctgct<br>agatgcccac<br>caaggtggcc<br>tattggaaa<br>cttgccctga<br>agaaaagaaa                                                          | ggaggtctat<br>cgaaattaat<br>ggtaccgagc<br>caagcaaagt<br>tctctctagg<br>ggtcatacca<br>ccttcttaaa<br>gctgtgctgt                                      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                                                                                                            | 60<br>120<br>180<br>240<br>300<br>360<br>420<br>480<br>540<br>600<br>660<br>720<br>780<br>840<br>900<br>960<br>1020                          |
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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                                                             | ataagcagag<br>acgactcact<br>tcggatccac<br>ggtggagcag<br>gtccacatctt<br>aaaaggagac<br>gctgggggtt<br>tcttgcactt<br>atggcccag<br>ccatgctagt<br>cgcaccagcc<br>cactttgctg<br>gagtgcagca<br>gaattcatg<br>acaagcaagt<br>aagcactaaa<br>acagtccaat                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 60<br>120<br>180<br>240<br>300<br>360<br>420<br>480<br>540<br>600<br>660<br>720<br>780<br>840<br>900<br>960<br>1020<br>1080                  |
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Leu Tyr Leu Ser Gln Pro Leu Thr His Thr Thr Ser Leu Leu Ala Gly

45

Burgara Andrews State Control of the State o Ile Gly Pro Val Leu Gly Leu Val Cys Val Pro Leu Leu Gly Ser Ala 40

| Se                     | r As<br>5  | p Hi<br>O  | s Tr       | p Ar       | g G1       | y Arg<br>5 |            | r Gl         | y Ar              | g Ar       | g Ar        |                   | o Pho              | e Il        | e Tr       |
|------------------------|------------|------------|------------|------------|------------|------------|------------|--------------|-------------------|------------|-------------|-------------------|--------------------|-------------|------------|
| A1<br>6                | a Le<br>5  | u Se       | r Le       | u Gl       | y 11       |            | ı Let      | ı Se:        | r Lei             | u Ph<br>7: |             | ı Ile             | e Pro              | Ar          | g Ala      |
| G1                     | y Tr       | р Le       | u Al       | a Gl<br>8  | y Le<br>5  | u Let      | ı Cys      | s Pro        | o Asp<br>90       |            | o Arq       | g Pro             | ) Let              | ı Glı<br>9! |            |
| Ala                    | a Le       | u Le       | u I1<br>10 | e Le<br>O  | u Gly      | y Val      | Gl3        | 7 Le:<br>105 |                   | ı Ası      | Ph€         | Cys               | Gly<br>110         |             | n Vai      |
| Cy                     | s Ph       | ₽ Th<br>11 | r Pr       | o Le       | u Glu      | a Alá      | Leu<br>120 | Lêu<br>)     | ı Ser             | Ası        | ) Lev       | 125               |                    | J Asp       | Pro        |
| Asp                    | 130        | s Cy:      | s Ar       | g Gli      | n Ala      | 135        | Ser        | · Val        | Tyr               | Ala        | 140         | Met               | Ile                | . Śér       | Leu        |
| Gl <sub>3</sub><br>145 | / Gly      | y Cy:      | s Le       | i Gly      | 7 Tyi      | : Lèu      | Leu        | Pro          | Ala               | 11e<br>155 |             | Trp               | Asp                | Thr         | Ser<br>160 |
| Ala                    | ı Leı      | ı Ala      | a Pro      | 165        | r, Lev     | Gly        | Thr        | Gln          | Glu<br>170        | Glu        | Ćys         | Leu               | Phe                | Gly<br>175  |            |
| Leu                    | Thr        | Le         | 180        | Phe        | e Leu      | Thr        | Cys        | Val<br>185   |                   | Ala        | Th <u>ŕ</u> | Leu               | Leu<br>190         |             | Ala        |
| Glu                    | Glu        | 195        | a Ala      | Leu        | Gly        | Prò        | Thr<br>200 | Glu          | Pro               | Ala        | Glü         | Glý<br>205        | Leu                | Seř<br>Sa   | Ala        |
| Pro                    | Ser<br>210 | Let        | ı Ser      | Pro        | His        | Суз<br>215 | Cys        | Pro          | Cys               | Arg        | Ala<br>220  | Arg               | Leu                | Ala         | Phe        |
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| Pro                    | Leu        | His        | Pro        | Gly<br>325 | Pro        | Asp        | Phe        | Ser          | Val<br>330        | Arg        | Lys         | <b>Val</b><br>∴∂∂ | <b>Gly</b><br>. :G | Met<br>335  | Asp        |
| Pro                    | Ile        | Cys        | Ile<br>340 | His        | Gly        | Phe        | Ser        | Trp          | Val               | Trp        | Asn         | Ile               | Ser                | Ala         | Суз        |

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| •                 | <211<br><212                         | 0> 63<br>L> 68<br>2> Pl<br>3> Ho                   | 34<br>RT                      | sapie                                    | ens                                     | . •                              |                                          | ž .;                                    |                                  | :                                        | 1                                   |                                      |                                           | ·                                      | ١. ٠٠٠                                    | . , .                                             |                                 |                          | 1. 1    |
|                   |                                      | )> 6:<br><b>M</b> et                               |                               | Ala                                      | Ser                                     | Lys                              | Glu                                      | Leu                                     | Gln                              | Val                                      | Leu                                 | 1                                    | Ile                                       |                                        | Phe                                       |                                                   |                                 |                          |         |
|                   |                                      |                                                    |                               |                                          |                                         | 1-7.**                           |                                          |                                         | ",£                              |                                          |                                     |                                      | . ب <sub>ا</sub> د                        |                                        | 15                                        |                                                   | •                               |                          | . : *   |
| 1                 | Asn                                  | Gln                                                | Asp                           | Asn<br>20                                | Ala                                     | Val                              | Ser                                      | His                                     | His<br>25                        | Thr                                      | Trp                                 | Glu                                  | Phe                                       | Gln<br>30                              | Thr                                       | Ser                                               |                                 |                          | . 17 1. |
| 5                 | Ser                                  | Pro                                                | <b>Val</b> 35                 |                                          | Arg                                     | Arg                              | Gly                                      | Gln<br>40                               | Val                              | Phe                                      | His                                 | Leu                                  | Arg<br>45                                 | Leu                                    | Val                                       | Leu                                               |                                 |                          |         |
| 1                 | Asn                                  | Gln<br>50                                          | Pro                           | Leu                                      | Gln                                     | Ser                              | Tyr                                      | His                                     | Gln                              | Leu                                      | Lys                                 | Leu                                  | Glu                                       | Phe                                    | Ser                                       | Thr                                               | -:                              |                          |         |
|                   |                                      | 50                                                 |                               |                                          | •••                                     | *.• *                            | ŞS                                       |                                         | 1 .                              | · :                                      | 554                                 | - 00                                 |                                           | . :                                    | ٠. ٤                                      |                                                   | ÷                               | •                        | •       |
| (                 | 31y<br>65                            | Pro                                                | Asn                           | Pro                                      | Ser                                     |                                  |                                          |                                         | His                              |                                          | Leu<br>75                           |                                      | Val                                       | Leu                                    | Asp                                       | 80                                                |                                 |                          |         |
| . 2               | Arg                                  | Thr                                                | Pro                           | Ser                                      | Asp<br>85                               | His                              | Tyr                                      | Asn                                     | Trp                              | Gln<br>90                                | Ala                                 | Thr                                  | Leu                                       | Gln                                    | Asn<br>95                                 | Glu                                               |                                 |                          | : 5     |
| :                 | Ser                                  | Gly                                                | Lys                           | Glu<br>100                               | Val                                     | Thr                              | Val                                      | Ala                                     | Val<br>105                       | Thr                                      | Ser                                 | Ser                                  | Pro                                       | Asn<br>110                             | Ala                                       | Ile                                               |                                 |                          |         |
| ]                 | Leu                                  | Gly                                                | Lys<br>115                    | Tyr                                      | Gln                                     | Leu                              | Asn                                      | Val<br>120                              | Lys                              | Thr                                      | Gly                                 | Asn                                  | His<br>125                                | Ile                                    | Leu                                       | Lys                                               |                                 |                          |         |
| 5                 | Ser                                  | Glu<br>130                                         | Glu                           | Asn                                      | Ile                                     | Leu                              | Tyr<br>135                               | Leu                                     | Leu                              | Phe                                      | Asn                                 | Pro                                  | Trp                                       | Суз                                    | Lys                                       | Glu                                               | • :                             |                          | ٠       |
| 7                 | N am                                 |                                                    | 17-1                          | Dho                                      | Mot                                     | :<br>Dmo                         |                                          | a`.<br>Glu                              | Nan                              | Clu                                      | N~~                                 | _;; ·                                | Gl n                                      | Merce                                  | т10                                       | Lon                                               | 17.25                           | 37)<br>19                | * ; *   |
|                   | 145                                  | Met                                                | val                           | rne                                      | Mec                                     | 150                              | _                                        |                                         | Asp                              |                                          | 155                                 | пуя                                  | GLU                                       | TAT                                    | Ile                                       | 160                                               |                                 | jvi.                     | 2.3     |
| 1                 | Asn                                  | Asp                                                | Thr                           | _                                        | _                                       |                                  | _                                        |                                         | _                                |                                          |                                     | _                                    |                                           |                                        | Lys<br>175                                | Cys                                               | eta di di                       |                          |         |
| 1                 | Lys                                  | Pro                                                | Trp                           | Asn                                      | Phe                                     | Gly                              | Gln                                      | Phe                                     | Glu                              | Lys                                      | Asn                                 | Val                                  | Leu                                       | Asp                                    | Cys                                       |                                                   |                                 |                          |         |
| ]                 | Ile                                  | Ser                                                |                               | Leu                                      | Thr                                     | <b>Glu</b>                       | Ser                                      | Ser                                     | Leu                              | Lys                                      | Pro                                 | Thr                                  | Asp                                       | Arg                                    | Arg                                       | Asp                                               |                                 |                          |         |
|                   |                                      |                                                    | 195                           | . s. J.                                  | •.•                                     | 1                                | ·:\                                      | 200                                     |                                  |                                          | : i .                               | : *:                                 | 205                                       | 7 1                                    | V135                                      | : 1                                               |                                 |                          |         |
| 1                 | Pro                                  | Val<br>210                                         | Leu                           | Val                                      | Cys                                     | Arg                              | Ala<br>215                               |                                         |                                  |                                          |                                     |                                      | Ser                                       |                                        |                                           | Lys                                               |                                 |                          |         |
| (                 | 31y                                  | Gln                                                | Gly                           | Val                                      | Leu                                     | Ile                              | GLy                                      |                                         |                                  | -                                        |                                     |                                      |                                           |                                        | Gly                                       |                                                   |                                 | `                        | •       |

|              | 225      |             |            |            |           | 230   |              |        |             | 77.       | 235                      | ٠.           |        |       |           | 240               |                                       |         |            |                |  |
|--------------|----------|-------------|------------|------------|-----------|-------|--------------|--------|-------------|-----------|--------------------------|--------------|--------|-------|-----------|-------------------|---------------------------------------|---------|------------|----------------|--|
| :            | Thr      | Δ1=         | Pro        | Tyr        | Lys       | Tro   | <b>ም</b> ስ ድ | Glv    | Ser         | Ala       | Pro                      | Tle          | Leu    | Gln   | Gln       | Tyr               |                                       |         | •          |                |  |
| el mario     |          |             |            |            |           |       |              |        |             |           |                          |              |        |       |           |                   | de la Constantina                     |         | ana na     | and the second |  |
| State of the |          |             |            |            |           |       |              |        |             |           |                          |              |        |       |           |                   |                                       |         | enereta d  |                |  |
|              | Tyr      | Asn         | Thr        | Lys<br>260 | Gln       | Ala   | . •          |        |             |           |                          |              | Trp    |       |           |                   |                                       | :       |            |                |  |
|              | -        |             |            |            | , -       | . '   | -            | 1.     |             | •         |                          |              |        |       | •         |                   |                                       |         | 1.         |                |  |
|              | Gly      | Ile         |            | Thr        | Thr       | Val   | Leu          |        |             | Leu       | Gly                      | Ile          |        | Ala   | Arg       | Ser               |                                       |         |            |                |  |
|              |          |             | 275        | -          |           |       |              | 280    | :           |           | •                        |              | 285    | , 1   |           |                   | 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 |         | •          |                |  |
|              | Val      |             | Gly        | Phe        | Asp       | Ser   | Ala          | His    | Asp         | Thr       | Glu                      |              | Asn    | Leu   | Thr       | Val               |                                       | 7       |            |                |  |
|              |          | 290         |            |            |           |       | 295          |        |             |           |                          | 300          |        |       | •         | . + 11            |                                       | · · · · | ţ.         |                |  |
|              | Asp      | Thr         | Tyr        | Val        | Asn       | Glu   | Asn          | Gly    | Lys         | Lys       | Ile                      | Thr          | Ser    | Met   | Thr       | His               | <b>,,</b> ,                           | s 2     | <i>:</i> . |                |  |
|              | 305      |             |            |            | 4.        | 310   |              | ę 4    | <u>.</u> .: | . 3°.     | 315                      | '            |        | . 23  | 4         | 320               | # . <del></del> .                     | 4 3.5   | 1.5        |                |  |
|              | Asp      | Ser         | Val        | Tro        | ੋ<br>Asn  | Phe   | His          | Val    | Tro         | Thr       | Asp                      | Ala          | Tro    | Met   | Ĺvs       | Ara               |                                       |         | • •        | •              |  |
|              |          |             |            |            |           |       | ٠٦           |        |             |           |                          |              |        |       |           |                   | في الم                                | · :     | j.         |                |  |
|              | Dwa      | <b>N</b> 0  | T 043      | Dwa        | Lys       | ٠.    |              |        |             |           | · ·.                     | ת ז ת        | 17-1   | 7 cm  | 7.1.0     | () )<br>The       |                                       |         |            |                |  |
|              | PLO      | Asp         |            |            | пув       |       |              |        |             |           | GTII                     | ыта          |        | 350   |           | 1111              | F S                                   |         |            |                |  |
|              |          |             |            |            |           |       |              | -      |             |           | _                        |              |        |       |           | _                 | 7.                                    | •       |            |                |  |
|              | Pro      | Gln         | Glu<br>355 | Arg        | Ser       | Gln   | Gly          | 360    | Phe         | Cys       |                          |              |        |       |           |                   |                                       |         |            | •              |  |
|              |          | •           |            |            | . 5       |       |              | × ,    |             |           |                          |              | 365    |       |           | # ·1              | € 2°E                                 | 1.5     | '          |                |  |
| ,            | Thr      |             | Ile        | Arg        | Lys       |       |              |        |             |           |                          |              |        |       |           |                   |                                       | •       |            |                |  |
|              |          | 370         |            | 2          | . •       | * 24  | 3/5          | . 'y   | į,          | -         | $\gamma \in \mathcal{J}$ | 380          | £ £.   | 1. T  | 16.0      | . • •             | f : \$                                |         | . •        |                |  |
|              |          | Phe         | Ser        | Glu        | Val       | Asn   | Gly          | Asp    | Arg         | Leu       | Ile                      | Trp          | Leu    | Val   | Lys       | Met               |                                       |         | •          | *              |  |
|              | 385      |             |            |            |           | 390   | ţ            | z      | 4.          |           | 395                      | . 8 -        |        | . : : | 722       | 400               | 2.17                                  | •       | , ž        |                |  |
|              | Val      | Asn         | Gly        | Gln        | Glu       | Glu   | Leu          | His    | Val         | Ile       | Ser                      | Met          | Glu    | Thr   | Thr       | Ser               | *                                     |         |            |                |  |
|              |          |             | _          |            | 405       |       |              |        |             |           |                          |              |        |       | 415       |                   |                                       |         |            |                |  |
|              | Tle      | GI v        | T.ve       | Δen        | Ile       | Ser   | Thr          | Lvs    | Δla         | ۷al       | Glv                      | Gln          | Asp    | Ara   | Ara       | Ara               |                                       |         |            |                |  |
|              |          | 013         | 230        | 420        |           |       | a.P.Y.       | _      | 425         |           |                          | 1.           |        | 430   | 9         |                   | ÷, +                                  |         |            |                |  |
|              | <b>3</b> | <b>-1</b> - | m\         |            | <b>63</b> |       | 3,           |        | D-1-0       | <b>61</b> | C1                       | G            |        | G3    | <b>61</b> | 7                 |                                       |         | •          |                |  |
|              | Asp      | тте         |            | -          | Glu       |       |              |        | Pro         |           | СΤΆ                      | ser          | 445    | GIU   | GIU       | Arg               | •                                     |         |            |                |  |
|              |          |             |            |            | •         |       |              | * 4    |             | . 5       |                          | ) * <u>.</u> |        | j.    |           |                   |                                       |         |            |                |  |
|              | Gln      | Val<br>450  | Met        | Asp        | His       | Ala   | Phe          | Leu    | Leu         | Leu       | Ser                      | Ser          | Glu    | Arg   | Glu       | His               |                                       |         | ٠          |                |  |
|              |          |             |            | , -        | ξ, τη     |       |              |        | *2.2        |           |                          |              |        |       |           | C!                |                                       |         |            |                |  |
|              | _        | Arg         | Pro        |            | Lys       | _     |              |        |             |           |                          |              |        |       |           |                   |                                       |         |            |                |  |
|              | 465      |             |            | ;')        | ryJ.      | 470   | 36 G         | · 1.   | 1.53        | r         | 475                      | ·5 a         |        | ŧ     | ر         | 480               | , P                                   | ₹       |            |                |  |
|              | Asp      | Val         | Leu        | Leu        | Gly       | Asn   | Ser          | Val    | Asn         | Phe       | Thr                      | Val          | Ile    | Leu   | Lys       | Arg               |                                       |         |            |                |  |
|              |          |             |            | ery i      | 485       | ( ).f | 0.04         | 25%    | as A        | 490       | (4)                      | C            | 5.3    | 7.1.5 | 495       |                   |                                       |         | ž5         |                |  |
|              | Lvs      | Thr         |            |            | Leu       |       |              |        |             |           |                          |              |        |       |           |                   |                                       |         |            |                |  |
|              | <u></u>  |             |            |            | 611       |       |              |        |             |           |                          |              |        |       |           |                   | 363                                   | 1.00    | . (2)      | •              |  |
|              | G1~      | Len         | Tire.      | ωρ~<br>,   | Gly       | Tare  | T.Ve         | Met    | 21-         | Tare      | Len                      | Cira         | Δen    | Leur  | 700       | Lare              |                                       |         |            |                |  |
|              | GTII     | TIER        | 515        | TIIL       | GTA       | цуэ.  | ··           | 520    |             | пλэ       | Heu.                     | ~ Ya         | 525    | neu   | A         | шуз               |                                       |         |            |                |  |
|              |          | _           |            |            |           |       |              | . ~ :  |             |           |                          |              | 210    |       |           |                   | i. **-                                | 45 F    | •          |                |  |
|              | Thr      | Ser<br>530  | Gln        | Ile        | Gln       |       |              |        |             |           |                          |              |        |       |           |                   |                                       |         |            |                |  |
|              |          |             |            |            | •         | •     | 7            | 13 3 m | ٧           | •         | . 4                      | 77.0         | i with | 277   | 1 1 1     | $\mathfrak{L}_BM$ | 1 3                                   | :       | ٠          |                |  |

Ser Lys Thr Tyr Ile Asn Ser Leu Ala Ile Leu Asp Asp Glu Pro Val 555 550 Ile Arg Gly Phe Ile Ile Ala Glu Ile Val Glu Ser Lys Glu Ile Met 570 Ala Ser Glu Val Phe Thr Ser Phe Gln Tyr Pro Glu Phe Ser Ile Glu - 585 Leu Pro Asn Thr Gly Arg Ile Gly Gln Leu Leu Val Cys Asn Cys Ile 600 Phe Lys Asn Thr Leu Ala Ile Pro Leu Thr Asp Val Lys Phe Ser Leu 615 Glu Ser Leu Gly Ile Ser Ser Leu Gln Thr Ser Asp His Gly Thr Val Gln Pro Gly Glu Thr Ile Gln Ser Gln Ile Lys Cys Thr Pro Ile Lys Thr Gly Pro Lys Lys Phe Ile Val Lys Leu Ser Ser Lys Gln Val Lys 665 660 Glu Ile Asn Ala Gln Lys Ile Val Leu Ile Thr Lys 680

<210> 633

<211> 679

<212> PRT

<213> Homo sapiens

<400> 633

Met Met Asp Ala Ser Lys Glu Leu Gln Val Leu His Ile Asp Phe Leu
5 10 15

The second state of

Asn Gln Asp Asn Ala Val Ser His His Thr Trp Glu Phe Gln Thr Ser 20 25 30

Ser Pro Val Phe Arg Arg Gly Gln Val Phe His Leu Arg Leu Val Leu 35 40 45

Asn Gln Pro Leu Gln Ser Tyr His Gln Leu Lys Leu Glu Phe Ser Thr
50 55 60

Gly Pro Asn Pro Ser Ile Ala Lys His Thr Leu Val Val Leu Asp Pro 65 70 75 80

Arg Thr Pro Ser Asp His Tyr Asn Trp Gln Ala Thr Leu Gln Asn Glu
85 90 95

Ser Gly Lys Glu Val Thr Val Ala Val Thr Ser Ser Pro Asn Ala Ile 100 105 110

Leu Gly Lys Tyr Gln Leu Asn Val Lys Thr Gly Asn His Ile Leu Lys
115 120 125

|                 | Ser        | Glu<br>130 | Glu        | Asn        | Ile        | Leu        | Tyr<br>135 | Leu        | Leu        | Phe        | Asn        | Pro<br>140    | Trp        | Cys        | Lys        | Glu         |     |   |        |     |                 |
|-----------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|---------------|------------|------------|------------|-------------|-----|---|--------|-----|-----------------|
| TORING TO STATE | Asp        | My to      | N.         | Pho        | 編          | P581       | A          | Glu        | ASA        |            | 159        | d <b>ys</b> , | S.W        |            | 利初         | Leu<br>160  |     |   | 8 1hay | ma) | <b>H</b> D)     |
|                 |            |            |            |            | Cys<br>165 |            |            |            |            |            |            |               |            |            |            |             |     |   |        |     |                 |
|                 | Lys        | Pro        | Trp        | Asn<br>180 | Phe        | Ģly        | Gln        | Phe        | Glu<br>185 | Lys        | Asn        | Val           | Leu        | Asp<br>190 | Cys        | Суз         | : • |   |        |     |                 |
|                 | Ile        |            | Leu<br>195 | Leu        | Thr        | Ģ1u        | Ser        | Ser<br>200 | Leu        | Lys        | Pro        | Thr           | Asp<br>205 | Arg        | Arg        | Asp         | ••. |   |        |     | * <b>A</b><br>1 |
|                 | Pro        | Val<br>210 | Leu        | Val        | Суя        | Arg        | Ala<br>215 | Met        | Çğs        | Ala        | Met        | Met<br>220    | Ser        | Phe        | Glu        | Lys         | *•  | • |        |     |                 |
|                 | Gly<br>225 | Gln        | Gly        | Val        | Leu        | 11e<br>230 | Gly        | Asn        | Trp        | Thr : 1    | Gly<br>235 | Asp           | Tyr        | Glu        | Gly        | Gly<br>240  |     |   | ٠      |     |                 |
|                 | Thr        | Ala        | Pro        | Tyr        | Lys<br>245 |            | Thr        | Gly        | Ser        | Ala<br>250 | Pro        | Ile           | Lęu        | Gln        | Gln<br>255 | Tyr         | ٠.  |   | .•     |     |                 |
|                 | Tyr        | Asn        | Thr        | Lys<br>260 | Gln        | Ala        | Val        | Cys        | Phe<br>265 | Gly        | Gln        | Cys           | Trp        | Val<br>270 | Phe        | Ala         |     |   |        |     |                 |
|                 | Gly        | Ile        | Leu<br>275 | Thr        | Thr        | Val        | Leu        | Arg<br>280 | Ala        | Leu        | Gly        | Ile<br>-      | Pro<br>285 | Ala        | Arg        | Ser         |     |   |        |     |                 |
|                 | Val        | Thr<br>290 | Gly        | Phe        | Asp        | Ser        | Ala<br>295 | His        | Asp        | Thr        | Glu        | Arg<br>300    | Asn        | Leu        | Thr        | Val         |     |   |        |     |                 |
|                 | Asp<br>305 | Thr        | Tyr        | Val        | Asn        | Glu<br>310 | Asn        | Gly        | Glu        | ГÀЗ        | Ile<br>315 | Thr           | Ser        | Met        | Thr        | His<br>320  |     |   | •      |     |                 |
|                 | Asp        | Ser        | Val        | Trp        | Asn<br>325 | Phe        | His        | Val        | Trp        | Thr<br>330 | Asp        | Ala           | Trp        | Met        | Lys<br>335 | Arg         |     |   |        |     |                 |
|                 | Pro        | Tyr        | Asp        | Gly<br>340 | Trp        | Gln<br>'   | Ala        | Val        | Asp<br>345 | Ala        | Thr        | Pro           | Gln        | Glu<br>350 | Arg        | Ser         |     |   |        |     |                 |
|                 | Gln        | Gly        |            |            | Cys        |            |            |            |            | Pro        | Leu        | Thr           | Ala<br>365 | Ile        | Arg        | Lys         |     |   |        |     |                 |
|                 | Gly        | Asp<br>370 |            | Phe        | Ile        | Val        | Tyr        | Asp        | Thr        |            |            | Val<br>380    |            |            | Glu        | Val         |     |   |        |     |                 |
|                 | Asn<br>385 |            | Asp        | Arg        | Leu        | Ile        | Trp        | Leu        | Val        | Lys        | Met        | Val           | Asn        | Gly        |            |             |     |   |        |     |                 |
|                 | Glu        | Leu        | His        | Val        | Ile<br>405 | Ser        | Met        | Glu        | Thr        | Thr        | Ser        | Ile           | Gly        | Lys        | Asn        | Ile         |     |   |        |     |                 |
|                 | Ser        | Thr        | Lys        |            | Val        | Gly        | Gln        | Asp        | Arg        | Arg        | Årg        | Asp           | Ile        | Thr        |            | <b>Gl</b> u |     |   |        |     |                 |
| ·               | Tyr        | Lys        | Tyr        | Pro        | Glu        |            |            |            |            |            |            |               |            |            |            | -           |     |   |        |     |                 |

|              |                  |           | ;      |          |          |                                         |              |                       |           |            |             |                    |              |                                         |              |
|--------------|------------------|-----------|--------|----------|----------|-----------------------------------------|--------------|-----------------------|-----------|------------|-------------|--------------------|--------------|-----------------------------------------|--------------|
| ,            |                  | 435       |        |          | :        |                                         | 440          |                       |           |            | , ,         | 445                |              |                                         |              |
| Ala          | Phe              | Len       | T.e.ii | T.em     | Ser      | Ser                                     | Glir         | Ara                   | Glii      | His        | Ara         | Gln                | Pro          | Val                                     | T.VS         |
|              | 450              | 100       | neu.   | Licu     | 501      | 455                                     |              | 1119                  | 024       | ,          | 460         | 024                | 120          | • • • • • • • • • • • • • • • • • • • • | 11,70        |
|              |                  | •         |        | -        |          |                                         |              |                       |           | •          | -,          |                    |              | • •                                     | * *          |
| Glu          | Asn              | Phe       | Leu    | His      | Met      | Ser                                     | Val          | Gln                   | Ser       | Asp        | Asp         | Val                | Leu          | Leu                                     | Gly          |
| 465          |                  |           |        |          | 470      |                                         | . 4          |                       |           | 475        |             | :                  |              |                                         | 480          |
| _            | _                |           |        | <u>.</u> |          |                                         |              |                       |           | _          | _           | •                  |              |                                         |              |
| Asn          | Ser              | .Va1      | Asn    |          | Thr      | Val                                     | Ile          | Leu                   |           | Arg        | Lys         | Thr                | ALa          |                                         | Leu          |
|              |                  | er er     |        | 485      |          | 10                                      |              |                       | 490       | L          |             | : - :              |              | 495                                     |              |
| Gln          | Asn              | Val       | Asn    | TIA      | Len      | GT v                                    | Ser          | Phe                   | Glar      | Len        | Gin         | Len                | Tur          | Thr                                     | GI v         |
| 0            |                  |           | 500    |          | ,        | V-1                                     | ,            | 505                   |           |            | <u> </u>    |                    | 510          | . 4.111                                 | Ų.           |
|              | •                |           |        |          |          |                                         |              |                       |           | · <u></u>  |             |                    |              | •                                       |              |
| Lys          | Lys              | Met       | Ala    | Lys      | Leu      | Cys                                     | Asp          | Leu                   | Asn       | Lys        | Thr         | Ser                | Gln          | Ile                                     | Gln          |
|              |                  | 515       |        |          |          |                                         | <b>520</b>   |                       | , 14 to 2 |            |             | 525                | : :          |                                         |              |
| ~3           |                  |           |        |          |          |                                         |              | en1                   | : 2       |            | _           |                    | -            |                                         |              |
| GLY          | Gln              | val       | Ser    | GTU      | val      | 7nr<br>535                              | Leu          | inr                   | теп       | Asp        |             | rys                | Thr          | Tyr                                     | TTE          |
|              | 530              |           |        | · · · .  |          | 333                                     | 14.          | 1.5                   | ::        | •          | 540         |                    | •.           |                                         |              |
| Asn          | Ser              | Leu       | Ala    | Ile      | Leu      | Asp                                     | Asp          | Glu                   | Pro       | Val        | Ile         | Ara                | Glv          | Phe                                     | Ile          |
| 545          |                  |           | • • •  |          | 550      | •                                       | <del>.</del> |                       | :. '      | 555        | ,           |                    |              |                                         | 560          |
|              |                  |           |        |          |          |                                         |              | - 11 4 4 4 1 1<br>- 1 | · · · · · | . 3        |             |                    |              |                                         |              |
| Ile          | Ala              | Glu       | Ile    |          | Glu      | Ser                                     | Lys          | Glu                   |           | Met        | Ala         | Ser                | Glu          |                                         | Phe          |
|              |                  |           |        | 565      |          |                                         | ю.           |                       | 570       |            | · ·         | 1.0                | .•           | 575                                     |              |
| mb ~         | 842              | Non.      | CIN    | 10 - 100 | Dwo      |                                         | Dho          | ė.                    | TIA       | C3.11      | ;<br>T. 017 | Ďто                | 7000         |                                         | C1           |
| 1111         | SeT              | ASII      | 580    | TAT      | PLO      | GIU                                     | FIIG         | 585                   | TTG       | Giu        | nea         | FIO                | 590          | 1111                                    | Gly          |
|              | 4,,50            |           |        | 73.34    |          |                                         | :            | 505                   |           | <b>.</b> . |             |                    |              |                                         |              |
| Arg          | Ile              | Gly       | Gln    | Léu      | Leu      | Val                                     | Cys          | Asn                   | Cys       | Ile        | Phe         | Lys                | Asn          | Thr                                     | Leu          |
| _            |                  | ,5°95     | •      |          |          |                                         | 600          | •                     |           |            |             | 605                |              |                                         |              |
|              | •                |           | _ '    |          | _ ;      | <b>_</b>                                |              |                       | ·<br>     |            | :           |                    | ·.           |                                         |              |
| Ala          | Ile              | Pro       | Leu    | Thr      | Asp      |                                         | ГÀЗ          | Phe                   | Ser       | Leu        |             | Ser                | Leu          | Gly                                     | Ile          |
|              | 610              |           | ;      |          |          | 615                                     | ٠.           | -                     | ٠.        |            | 620         | **.                |              |                                         |              |
| Ser          | Ser              | Ten       | GIn    | Thr      | Ser      | Asp                                     | His          | GI v                  | Thr       | Va1        | Gln         | Pro                | Glv          | Glu                                     | Thr          |
| 625          |                  | ,         |        |          | 630      | ,                                       |              |                       | -,,       | 635        |             | -,                 | <u></u>      |                                         | 640          |
|              |                  |           |        |          | -        | ·                                       |              |                       |           |            | • • •       |                    |              |                                         |              |
| Ile          | Gln              | Ser       | Gln    | Ile      | Lýs      | Cys                                     | Thr          | Pro                   | Ile       | Lys        | Thr         | Gly                | Pro          | Lys                                     | Lys          |
|              |                  |           |        | 645      |          |                                         | •            |                       | 650       |            |             |                    |              | 655                                     |              |
| Dh.          | T1.              | T7_ 1     | T      | T        | 0        |                                         | ·T           | <b>C1</b>             |           | <b>-</b>   | <u></u>     | T1 -               | ź            | 73.T.                                   | <b>C1</b> -  |
| Pne          | Ile              | vaı       | тÃв    | теп      | ser      | ser                                     | тАг          | 651II                 | vaı       | тля        | GIU         |                    |              |                                         | GIN          |
|              |                  |           | 900    |          | •        |                                         | 7 P. P.      | 003                   |           | :          | 1 4 4       |                    | .670         |                                         |              |
| Lys          | Ile              | Val       | Leu    | Ile      | Thr      | Lys                                     | 41. 1        | . :                   |           |            |             |                    |              |                                         | 1₹<br>Stanta |
| _            |                  | 675       |        | -        |          | - 45<br>- 1                             |              |                       |           |            |             |                    |              |                                         | · ·          |
|              | -                | ·.        |        |          |          |                                         |              |                       |           | 2.1        |             | istoria<br>Istoria |              |                                         |              |
|              |                  |           |        | · . ,    |          |                                         |              |                       |           |            |             |                    | 5 i          | :                                       |              |
| Z017         | 0> 63            | 2.4 :     | . 6 15 |          | <u> </u> |                                         | Sec. 15      | :                     |           | •          |             |                    | • •.         |                                         |              |
| <211<br><211 | // 0.3<br>  5 54 | 54<br>562 | . 4    |          | -        | . * *                                   |              |                       | .•        |            |             | *                  | i 🦿          |                                         |              |
| <212         | L> 56<br>2> D1   | IA.       |        | . \ :    | . :      | • • • • • • • • • • • • • • • • • • • • | . :          | - " :                 | * 1 1 1   | 1.75       |             | 1 12               | . **         |                                         | (A) 2        |
| <213         | 3> Ho            | omo s     | sapie  | ns       | 2        | • • •                                   |              |                       | • • •     |            | • * :       |                    | ,            |                                         |              |
|              |                  |           |        | **       |          |                                         |              |                       |           |            |             |                    | e et<br>Vite | 1111                                    |              |
| <400         | 0> 63            | 34        |        |          |          |                                         |              | - 1                   |           |            | ٠.          |                    |              |                                         |              |
| gtca         | actta            | agg a     | adaac  | gtat     | tc ct    | ttc                                     | ggca         | a gc                  | eggge     | ctca       | gcat        | tgagg              | gaa (        | cagaa                                   | aggaat       |

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Ser Ser Ala Ser Arg Ser Thr Asp Leu Ser Tyr Ser Glu Ser Asp Leu
           Val Asn Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe
            40
                                total tell sold side for
Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala
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Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp

Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp

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|           |        |             |             |               |           |        |              |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | ,        |                                        |          |                                 |           |               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
|-----------|--------|-------------|-------------|---------------|-----------|--------|--------------|-------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|----------------------------------------|----------|---------------------------------|-----------|---------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|
| Tlo       | ~1 n   | Dho         | C1::        | ሞትኍ           |           |        |              |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |          |                                        |          |                                 |           | Ser           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
| TTG       | GTII   | FITE        | 100         | 1111          | пеп       | GTA    | Llys         | 105   | 0.1.4                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |          | -1-                                    |          | 110                             | 1, 2.     |               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
|           |        |             |             |               |           |        |              |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |          |                                        |          |                                 |           |               | n nedalizativ                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |   |
| Cys       | Asp    | Thr         | Asp         | Ala           | Glu       | Ile    | Leu          | Tyr   | Glu                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Leu      | Leu                                    | Thr      | Gln                             | His       | Trp           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
| _         | _      | 115         |             |               |           | ∵ .    | 120          | + 2 5 | :                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | સુર્જ ડો |                                        | 125      |                                 | 1.00      | 1577          | ។ ខេត្តបានប្រជាជា                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |   |
|           | • • •  |             | •           | ·             |           |        |              |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |          |                                        |          |                                 |           | .:            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
| His       |        | Гуз         | Thr         | Pro           | Asn       | Leu    | Val          | Ile   | Ser                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Val      | Thr                                    | GLY      | Gly                             | .Ala      | Lys           | in the state of the control of the state of |   |
| 1         | 130    | , •         | 17.         |               |           | 135    | • • • •      |       | in the same of the | 2.4      | TÃO                                    |          | .a. i                           |           |               | s dalesta ya<br>Nemala dalesi                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |   |
| 7         | Dha    |             |             |               |           |        |              |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |          |                                        |          |                                 |           |               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
| 145       | Fire   | ALG         | пеа         | цуэ           | 150       | nr.g   | Hec          | arg.  | Lys.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 155      | 2110                                   |          | 7.5                             | - <b></b> | 160           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
| 740       | ., • • | +.          | 350         |               | 13.       | 3 73   |              | 90. · | ia uni                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |          |                                        | . to 1 Z | F. 3                            | 34.31     | - E:          | រី ខេត្តទៅស្រាស់។<br>រ                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |   |
| Tyr       | Ile    | Ala         | Gln-        | Ser           | Lys       | Gly    | Ala          | Trp   | Ile                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Leu      | Thr                                    | Gly      | Gly                             | Thr       | His:          | 1 - 1 - 1 - 2 5T                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | • |
|           |        | <b>L</b> 10 | 4 . 97      | 165           |           | ្រាវ   | 30 t         | 1=    | 170                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 5 S G    | n Port :                               | to a     | , -                             | 175       | ومرز شاه      | to tack at Market                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |   |
|           |        |             |             |               |           |        |              |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |          |                                        |          |                                 |           |               | r Augusturys                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |   |
| Tyr       | Gly    | Leu         | Thr         | Lys           | Tyr       | Ile    | Gly          | Glu   | Val                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Val.     | Arg                                    | Asp      | Asn                             | Thr       | Ile           | ซ ค <sub>ือที่</sub> คล เกาน                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |   |
|           |        |             |             |               |           |        |              |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |          |                                        |          |                                 |           |               | గ్రామండి ఉన్నాయి.<br>గ్రామం                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |   |
| 80~       |        |             |             |               |           |        |              |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |          |                                        |          |                                 |           |               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
| per       | ALG    | 195         | Ser         | GIU           | Gru       | PESII. | 200          | .463  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |          | :::::::::::::::::::::::::::::::::::::: | 205.     |                                 |           | . <b></b><br> | i de la companya de<br>Se la companya de la                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
| •         | 100    |             |             |               |           |        |              |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |          |                                        |          |                                 |           |               | e a lu f                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |   |
| Gly       | Met    | Val         | Ser         | Asn           | Arg       | Asp    | Thr          | Leu   | Ile                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Arg      | Asn                                    | Cys      | Asp                             | Ala       | Glu           | Sold from the second                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |   |
| _         |        |             |             |               |           |        |              |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |          |                                        |          |                                 |           |               | · · · · · · · · · · · · · · · · · · ·                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |   |
|           |        |             |             |               |           |        |              |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |          |                                        |          |                                 |           |               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
| _         |        | Phe         | Leu         | Ala           | Gin       | Tyr    | Leu          | Met   | Asp                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Asp      | Phe                                    | rnr      | Arg                             | Asp       | Pro           | o miliota de la comercia.<br>A collingua en Collega                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |   |
| 225       |        |             |             |               |           |        |              |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |          |                                        |          |                                 |           |               | र (१४०)<br>१ १६८७६ - १                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |   |
| Ten       | Tyr    | Tie         | Leu         | Asp           | Asn       | Asn    | His          | Thr   | His                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Leu      | Leu                                    | Leu      | .Val                            | Asp       | Asn           | s udinokhurs                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |   |
| Lou       |        |             | 7.          | 245           | //        | 7      | 9 /          |       | 250                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 84       |                                        | in Ji    | i j                             | 255       | 10011         | າ<br>ກ່ອງເຄຍ                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |   |
|           | . :    |             |             | • ;           |           | , ,    | 0.0          | 12 3  | · j::                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 4 1      | 1351 s                                 | *        | ; ; .                           | 1150      | 1-2.5         | y gudeffort -                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |   |
| Gly       | Cys    | His         | Gly         | His           | Pro       | Thr    | Val          | Glu   | Ala                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Lys      | Leu                                    | Arg      | Asn                             | Gln       | Leu           | $-\tau_i \mathcal{D}_{i_i}(x_i, \tilde{x}_i) \in \mathcal{T}_{i_i}$                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |   |
|           |        |             | 260         | 42.7          |           |        | •            | 265   | N = 30                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |          | £                                      | -        | 270                             | 4.8       | 7.5           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
| <b>63</b> |        |             | <b>-</b> 1- |               | <b>63</b> | 7      | m\           | T1.   | C1 ~                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 7.00     | ).<br>Go∞                              | N on     | m                               | C3 **     |               | 659 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |   |
| GIU       | гĀS    | H1S<br>275  | TTE         | ser           | GIU       | Arg    | 280          | TTE   | GTII                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | ASP      | Ser                                    | 285      | TÄT                             | GTĀ       | Gly           | •                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 1 |
|           |        | 213         |             |               |           |        | 200          |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |          |                                        | 200      |                                 |           |               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
| Lvs       | Ile    | Pro         | Ile         | Val           | Cys       | Phe    | Ala          | Gln   | Gly                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Gly      | Gly                                    | Lys      | Glu                             | Thr       | Leu           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
| -4 -      | 290    |             |             |               | -         | 295    |              |       | -                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | _        | 300                                    | _        |                                 |           | ) .           | \$ 100                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |   |
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|           | Ala    | Ile         | Asn         | Thr           | Ser       | Ile    |              | Asn   | Lys                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |          |                                        |          |                                 |           |               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
| 305       |        |             |             | ·             | 310       |        | 1            |       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 315      | £.                                     |          | 2 * 14                          |           | 320           | . 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |   |
| C1        | C3 ++  | e~~         | C1 **       | .)<br>- 70 mm | Tla       | 70.7 = | Men          | Val   | <i>Ji</i> ∵<br>Tle                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Z 7 2    | Ser                                    | T.e.ii   | Val                             | Glas      | Val           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
| GIU       | СТУ    | Ser         |             |               |           |        |              | Val.  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |          |                                        |          |                                 |           |               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
| . :       |        |             |             | 020           | į., ;     |        |              | 1.    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 4.       |                                        |          |                                 |           |               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
| Glu       | Asp    | Ala         | Pro         | Thr           | Ser       | Ser    | Ala          | Val   | Lys                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Glu      | Lys                                    | Leu      | Val                             | Arg       | Phe           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
|           | -      |             |             |               |           |        |              | 345   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |          |                                        |          |                                 |           | •             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
|           |        |             | _           |               | _         | :      | _            | _     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |          |                                        |          |                                 | _         | _             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
| Leu       | Pro    | Arg         | Thr         | Val           | Ser       | Arg    | Leu          | Ser   | GLu                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | GLU      | GLu                                    | Thr      | GLU                             | Ser       | Trp           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
|           |        | 305         | 2           | • • •         | 1 9/      | ₹.     | <i>⊃</i> ,0∪ | 7.3   | 23.57                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | e et e   | ال. أناس                               | 3.03     | ¥. ^                            |           | 6.3           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
| Tla       | Tare   | Tro         | T.e.        | T.ve          | G1 11     | I)e    | Len          | Glu   | Cvs                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Ser      | His                                    | Lev      | Leu                             | Thr       | Val           | 33                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | • |
| *76       | 370    | P           | -L-u        | - <b> </b>    | <u> </u>  | 375    | V.(.)        | 373.4 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | S. vi    | 380                                    | 713      | 930                             |           | 3 1-21        | A 6 5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |   |
|           | •      |             |             | •             |           |        |              | ř.    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | • •      |                                        |          | Ti V                            |           | **            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
| Ile       | Lys    | Met         | Glu         | Glu           | Ala       | Gly    | Asp          | Glu   | Ile                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Val      | Ser                                    | Asn      | Ala                             | Ile       | Ser           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |
| 385       |        |             |             |               | 390       |        | : '          | . 7   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 395      | : 65                                   |          | $\cdot_{\lambda,\mathbf{t}}(z)$ |           | 400           | 14 - 12 - 12                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |   |
|           |        |             |             |               |           |        |              |       | 2.5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |          |                                        |          |                                 |           |               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |   |

|             | 1114       | Dog        | -7-        | 405        | ma         |            | 501        | +411       | 410        | Olu        | 0,111      | .mp               | my o       | 415        | 21011      |             | •              |          |
|-------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------------|------------|------------|------------|-------------|----------------|----------|
| Trp         | Asn        | Gly        | Gln<br>420 | Leu        | Lys        | Leu        | Leu        | Leu<br>425 | Glu        | Trp        | Asn        | Gln               | Leu<br>430 | Asp        | Leu        |             | -              |          |
| Ala         | Asn        | Asp<br>435 | Glu        | Ile        | Phe        | Thr        | Asn<br>440 | Asp        | Arg        | Arg        | Trp        | Glu<br>445        | Ser        | Ala        | Asp        |             | _              |          |
| Leu         | Gln<br>450 | Glu        | Val        | Met        | Phe        | Thr<br>455 | Ala        | Leu        | Ile        | Lys        | Asp<br>460 | Arg               | Pro        | ГÀЗ        | Phe        |             | •              | •        |
| Val<br>465  | Arg        | Leu        | Phe        | Leu        | Glu<br>470 | Asn        | GLy        | Leu        | Asn        | Leu<br>475 | Arg        | Lys               | Phe        | Leu        | Thr<br>480 |             |                |          |
| His         | Asp        | Val        | Leu        | Thr<br>485 |            |            |            |            | Asn<br>490 | His        | Phe        | Ser               | Thr        | Leu<br>495 | Val        |             | . !            |          |
| Tyr         | Arg        | Asn        | Leu<br>500 | Gln        |            |            | Lys        |            | Ser        | Tyr        | Asn        | Asp               | Ala<br>510 | Leu        | Leu        |             | •              | ı        |
| Thr         | Phe        | Val<br>515 | Trp        | Lys        | Leu        | Val        | Ala<br>520 | Asn        | Phe        | Arg        | Arg        | Gly<br>525        | Phe        | Arg        | Lys        |             |                |          |
| <b>Gl</b> u | Asp<br>530 | Arg        | Asn        | Gly        | Arg        | Asp<br>535 | Glu        | Met        | Asp        | Ile        | Glu<br>540 | Leu               | His        | Asp        | Val        | atri<br>NGS |                | • ;      |
| Ser<br>545  | Pro        | Ile        | Thr        | Arg        | His<br>550 | Pro        | Leu        | Gln        | Ala        | Leu<br>555 | Phe        | Ile               | Trp        | Ala        | Ile<br>560 | •           | ٠.             |          |
| Leu         | Gln        | Asn        | Lys        | Lys<br>565 | Glu        | Leu        | Ser        | Lys        | Val<br>570 | Ile        | Trp        | Glu               | Gln        | Thr<br>575 | Arg        |             | •              |          |
| Gly         | Cys        | Thr        | Leu<br>580 | Ala        | Ala        | Leu        | Gly        | Ala<br>585 | Ser        | Lys        | Leu        | Leu               | Lys<br>590 | Thr        | Leu        | : :         | •              |          |
| Ala         | Lys        | Val<br>595 | Lys        | Asn        | Asp        | Île        | Asn<br>600 | Ala        | Ala        | Gly        | Glu        | Ser<br>605        | Glu        | Glu        | Leu        |             |                | •        |
| Ala         | Asn<br>610 | Glu        | Tyr        | Glu        | Thr        | Arg<br>615 | Ala        | Va1        | Glu        | Leu        | Phe<br>620 | Thr               | Glu        | Cys        | Tyr        |             |                | . ,      |
| Ser<br>625  | Ser        | Asp        |            | Asp        |            |            |            |            |            | 635        |            | _                 |            | _          | 640        | 3 + ±       | 1 4 1<br>1 1 2 | e prince |
| Ala         | Trp        | Gly        | Gly        | Ser<br>645 | Asn        | Cys        | Leu        | Glu        | Leu<br>650 | Ala        | Val        | Glu               | Ala        | Thr<br>655 |            |             |                |          |
| Gln         | His        | Phe        | Thr<br>660 |            |            |            | Gly        | Val<br>665 | Gln        | Asn        | Phe        | Leu               | Ser<br>670 | Lys        | Gln        | 7.7         |                | ٠        |
| Trp         | Tyr        | Gly<br>675 | Glu        |            | Ser        |            | Asp<br>680 | Thr        |            |            |            | <b>Lys</b><br>685 |            | Ile        | Leu        | ٠.          |                | .*       |
| Суз         | Leu<br>690 | Phe        | Ile        | Ile        | Pro        | Leu<br>695 |            | Gly        | Cys        | GLY        | Phe<br>700 |                   |            |            | Arg        |             |                |          |
| īvs         | Lvs        | Pro        | Va 1       | Asp        | ī.vs       | His        | Lvs        | Lvs        | Len        | Leu        | Tro        | Tvr               | Tyr        | Val        | Ala        |             |                | •        |

service of the

| 705        | •           |            |            | ı          | 710                          |                          |             | •                       | · ,        | 715            | : •                      |             | •:                       |            | 720        |                   |
|------------|-------------|------------|------------|------------|------------------------------|--------------------------|-------------|-------------------------|------------|----------------|--------------------------|-------------|--------------------------|------------|------------|-------------------|
| Phe        | Phe         | Thr        | Ser        |            | Phe                          | Val                      |             | Phe                     | Ser<br>730 | Trp            | Asn                      | Val         | Val                      | Phe<br>735 | Tyr        |                   |
| Ile        | Ala         | Phe        | Leu<br>740 | Leu        | Leu                          | Phe                      | Ala         | Tyr<br>745              | Val        | Leu            | Leu                      | Met         | Asp<br>750               | Phe        | His        | :                 |
| Ser        | Val         | Pro<br>755 | His        | Pro        | Pro                          | Glu                      | Leu<br>760  | Val                     | Leu        | Tyr            | Ser                      |             |                          | Phe        | Val        |                   |
| Leu        | Phe<br>770  | _          | Asp        | Glu        | <b>Val</b>                   | Arg<br>775               | 10 m        | Trp                     | Tyr        | Val            | Asn<br>780               | 1.23        | Val                      | Asn        | Tyr        |                   |
| Phe<br>785 | Thr         | Asp        | Leu        | Trp        | Asn<br>790                   | <b>Val</b>               | Met         | Asp                     | Thr        | Leu<br>795     | <b>Gly</b><br>209        | Leu<br>19 û | Phe                      | <b>Tyr</b> | Phe<br>800 | \$ <b>,</b> W     |
| Ile        | Ala         | Gly        |            | Val<br>805 |                              | Arg                      | Leu         | His<br>: <sub>V</sub> i | Ser<br>810 | Ser            | Asn                      | Lys         | Ser                      | Ser<br>815 | Leu        | , 4. <sup>5</sup> |
| Tyr        | Ser         | Gly        | Arg<br>820 | Val        | Ile                          | Phe                      | Cys<br>:    | Leu<br>825              | Asp        | Tyr            | Ile<br>314<br>317        | Ile         | Phe<br>830               | Thr        | Leu        | 1, w/y<br>et      |
| Arg        | Leu         | Ile<br>835 | His        | Ile<br>grá | Phe                          | Thr                      | Val<br>840  |                         | Arg        | Asn<br>:       | Leu                      | Gly<br>845  | Pro                      | Lys        | Ile        |                   |
| Ile        | Met<br>850  | Leu        | Gln        | Arg        | Met                          | Leu<br>855               | Ile         | Asp                     | Val        | Phe            | Phe<br>860               | Phe         | <b>Leu</b><br>८६५<br>६८३ | Phe<br>955 | Leu        | 315               |
| Phe<br>865 | Ala         | Val        | Trp        | Met        | Val<br>870                   | Ala                      | Phe         | Gly                     | <b>Val</b> | Ala<br>875     | Arg                      | Gln         | Gly                      | Ile        | 880<br>Leu | I                 |
| Arg        | Gln         | Asn        | <b>Glu</b> | Gln<br>885 | <b>Arg</b><br>- 7 1<br>0 - 1 | Trp                      | Arg         | Trp                     | Ile<br>890 | Phe            | Arg                      | Ser         | Val                      | Ile<br>895 | Tyr        |                   |
| Glu        | Pro         | Tyr        | Leu<br>900 | Ala        | Met                          | Phe                      | Gly         | Gln<br>905              | Val        | Pro            | Ser                      | Asp         | Val<br>910               | Asp        | Gly        |                   |
| Thr        | Thr         | Tyr<br>915 |            |            | Ala                          | His                      | Cys<br>920  |                         | Phe        | Thr            | GJA                      | Asn<br>925  | Glu                      | Ser        | Lys        |                   |
| Pro        | Leu<br>930  | Суз        | Val        | Glu        | Leu<br>3-d                   | Asp<br>935               | Glu         | His                     | Asn        | Leu            | Pro<br>940               | Arg         | Phe                      | Pro        | Glu        |                   |
| Trp<br>945 | Ile         | Thr        | Ile<br>« 4 | Pro (1952) | Leu<br>950                   | Val                      | Cys         | Ile                     | Tyr        | Met<br>955     | Leu                      | Ser         | Thr                      | Asn        | 11e<br>960 |                   |
| Leu        | Leu         | Val        | Asn        | Leu<br>965 | Leu<br>118 m<br>L d          | Val                      | Ala         | Met                     | Phe<br>970 | Gly            | Tyr                      | Thr<br>John | Val                      | Gly<br>975 | Thr        | į .               |
| Va1        | Gln         | Glu        | Asn<br>980 | Asn        | Asp                          | <b>Gln</b><br>공항상<br>공사원 | Val         | Trp<br>985              | FÅY<br>FÅY | Phe            | <b>Gln</b><br>2.3<br>9/3 | Arg         | Tyr<br>990               | Phe        | Leu<br>(-) | 44. V             |
| Val        | Gln         | Glu<br>995 | Tyr        | Cys        | Ser                          | Arg                      | Leu<br>1000 | Asn                     | Ile        | <b>Pro</b> 710 | Phe                      | Pro<br>100  | Phe<br>5000              | Ile        | Val        | ્ગુતાર            |
| Phe        | Àla<br>1010 |            | Phe        | Tyr        | Met                          | Val<br>101               | Val         | Lys                     | Lys        | Cys<br>;       | Phe<br>102               | Lys<br>Jadi | <b>Cys</b><br>ලෝ         | Cys        | Суз        | $Q \cdot Q$       |

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|            |            |            | 100        |            | ı          |            |            | 105        | , ,        |            | ,          |            | 110        |            |            |
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| Cys        | Asp        | Thr<br>115 | Asp        | Ala        | Glu        | Ile        | Leu<br>120 | Tyr        | Glu        | Leu        | Leu        | Thr<br>125 | Gln        | His        | Trp        |
| His        | Leu<br>130 | Lys        | Thr        | Pro        | Asn        | Leu<br>135 | Val        | Ile<br>;   | Ser        | Val        | Thr<br>140 | Gly        | Gly        | Ala        | Lys        |
| Asn<br>145 | Phe        | Ala        | Leu        | Lys        | Pro<br>150 | Arg        | Met        | Arg        | Lys        | Ile<br>155 | Phe<br>,   | Ser        | Arg        | Leu        | 11e<br>160 |
| Tyr        | Ile        | Ala        | Gln        | Ser<br>165 | Lys        | Gly        | Ala        | Trp        | Ile<br>170 | Leu        | Thr        | Gly        | Gly        | Thr<br>175 | His        |
| Tyr        | Gly        | Leu        | Met<br>180 | _          | Tyr        | Ile        | Gly        | Glu<br>185 |            | Va1        | Arg        | Asp        | Asn<br>190 | Thr        | Ile        |
| Ser        | Arg        | Ser<br>195 | Ser        | Glu        | Glu        |            | 11e<br>200 |            | Ala        |            | Gly        | 11e<br>205 |            | Ala        | Trp        |
| Gly        | Met<br>210 | Val        | Ser        | Asn<br>    | Arg        | Asp<br>215 | Thr        | Leu        | Ile        | Arg        | Asn<br>220 | Суз        | Asp        | Ala        | Glu        |
| Gly<br>225 | Tyr        | Phe        | Leu        | Ala        | Gln<br>230 | Tyr        | Leu        | Met        | Asp        | Asp<br>235 |            | Thr        | Arg        | Asp        | Pro<br>240 |
| Leu        | Tyr        | Ile        | Leu        | Asp<br>245 |            | Asn        |            | Thr        | His<br>250 | Leu        | Leu        | Leu        | Val        | Asp<br>255 | Asn        |
| Gly        | Cys        | His        | Gly<br>260 |            | Pro        | Thr        | Val        | Glu<br>265 | Ala        | Lys        | Leu        | Arg        | Asn<br>270 | Gln        | Leu        |
| Glu        | Lys        | Tyr<br>275 | Ile        | Ser        | Glu        | Arg        | Thr<br>280 | Ile        | Gln        | Asp        | Ser        | Asn<br>285 | Tyr        | Gly        | Gly        |
| Lys        | 11e<br>290 | Pro        | Ile        | Val        | Суѕ        | Phe<br>295 | Ala        | Gln        | Gly        | Gly        | 300<br>300 | Lys        | Glu        | Thr        | Leu        |
| Lys<br>305 | Ala        | Ile        | Asn<br>    | Thr        | Ser<br>310 | Ile        | Lys        | Asn        |            | Ile<br>315 |            | Сув        | Val        | Val        | Val<br>320 |
| Glu        | Gly        | Ser        | Gly        | Gln<br>325 |            | Ala        | Asp        | Val        | 11e<br>330 | Ala        | Ser        | Leu        | Val        | Glu<br>335 | Val        |
| Glu        | Asp        | Ala        | Leu<br>340 |            |            |            |            |            |            |            |            | Leu        |            | Arg        | Phe        |
| Leu        | Pro        | Arg<br>355 | Thr        |            |            | Arg        |            |            |            |            |            | Thr<br>365 |            |            | Trp        |
| Ile        | Lys<br>370 | Trp        | Leu        | Lys        |            | 11e<br>375 |            |            |            |            |            |            | Leu        |            | Val        |
| Ile<br>385 | Lys        | Met        | Glu        |            | Ala<br>390 | _          |            |            |            |            |            |            |            |            | Ser<br>400 |
| Tyr        | Ala        | Leu        | Tyr        | Lys<br>405 | Ala        | Phe        | Ser        | Thr        | Ser<br>410 | Glu        | Gln        | Asp        | Lys        | Asp<br>415 | Asn        |

|            |            |            |            |            | ſ          |            |                  |            | 1          |            |             |            |            |            |            |                               |
|------------|------------|------------|------------|------------|------------|------------|------------------|------------|------------|------------|-------------|------------|------------|------------|------------|-------------------------------|
| Trp        | Asn        | Gly        | Gln<br>420 | Leu        | Lys        | Leu        | Leu              | Leu<br>425 | Glu        | Trp        | Asņ         | Gln        | Leu<br>430 | Asp        | Leu        |                               |
| Ala        | Asn        | Asp<br>435 | Glu        | Ile        | Phe        |            | Asn<br>440       | <b>Asp</b> | _          | _          | Trp         |            |            | Ala        | Asp        |                               |
| Leu        | Gln<br>450 | Glu        | Val        | Met        | Phe        | Thr<br>455 | Ala              |            |            | Lys        | Asp<br>460  | -          |            | Lys        | Phe        |                               |
| Val<br>465 | Arg        | Leu        | Phe        |            |            |            | _                |            |            |            | Arg         | Lys        | Phe        |            |            | •                             |
| His        | Asp        | Val        |            |            |            |            |                  |            |            |            | Phe         |            |            |            | Val        |                               |
| Tyr        | Arg        | Asn        |            | Gln'       | Ile        | _          | Lys              | Asn        | Ser        | Tyr        | Asn         | Asp        |            |            | 5. 5       |                               |
| Thr        | Phe        | Val<br>515 | Trp        | Lys        | Leu        | Val        | Ala<br>520       | Asn        |            |            | Arg         |            |            |            | Lys        |                               |
| Glu        | Asp<br>530 | Arg        |            | Gly        | 1          | Asp<br>535 |                  | Met        | Asp        |            | Glu<br>540, | Leu        | His        | Asp        | <b>Va1</b> |                               |
| Ser<br>545 | Pro        | Ile        | Thr        | Arg        |            |            |                  |            |            |            | Pheii       |            | _          |            |            |                               |
| Leu        | Gŀn        | Asn        | <b>Lys</b> | Lys<br>565 | Glu<br>;   | Leu        | Ser              |            | Val<br>570 |            | Trp         |            |            |            | -          | $\sim T_{\rm e} m r^{\prime}$ |
| Gly        | Cys        | Thr        | Leu<br>580 | Ala        | Ala        |            | Gly<br>:         | Ala<br>585 |            | Lys        | Leu         | Leu        | Lys<br>590 | Thr        | Leu        |                               |
| Ala        | Lys        | Val<br>595 | Lys        | Asn        | Asp        | Ile        | 600              | Ala        | Ala        | Gly        | Glu         | Ser<br>605 | Glu        | Glu        | Leu        |                               |
| Ala        | Asn<br>610 | Glu        | Tyr        | Glu        | Thr        | Arg<br>615 | Alà <sup>c</sup> | Val        | Glu        | Leu        | Phe<br>620  | Thr        | Glu        | Суз        | Tyr        |                               |
| Ser<br>625 | Ser        | Asp        | Glu        | Asp        | Leu<br>630 | Ala        | Glu              | Gln        |            | Leu<br>635 | Val         | Tyr        | Ser        | Суѕ        | Glu<br>640 |                               |
| Ala        | Trp        | Gly        | Gly        |            |            | _          |                  | Glu        |            |            | Val         |            |            | Thr<br>655 | Asp        | ž-1-21                        |
| Gln        | His        | Phe        |            |            |            |            |                  |            |            |            | Phe         |            |            |            |            |                               |
| ·Trp       | Tyr        | Gly<br>675 |            |            |            |            |                  |            |            |            |             |            |            |            |            | esti                          |
| Cys        | Leu<br>690 | Phe        | Ile        | Ile        |            |            |                  | _          | -          |            | Phe<br>700  |            |            |            | _          | en Sign                       |
| Lys<br>705 | Lys        | Pro        | Val        |            | 710        | His        |                  |            | Leu        | Leu<br>715 | Trp         | Tyr<br>260 | Týr        | Val        | Ala<br>720 | . 1 - 12.                     |

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| Phe Phe Thr         | Ser Pro<br>725 |               | l Val        | Phe        | Ser<br>730 | _          | Asn        | Val         | Val         | Phe<br>735 | Tyr        |
|---------------------|----------------|---------------|--------------|------------|------------|------------|------------|-------------|-------------|------------|------------|
| Ile Ala Phe         | Leu Leu<br>740 | Leu Ph        | e Ala        | Tyr<br>745 | Val        | Leu        | Leu        | Met         | .Asp<br>750 | Phe        | His        |
| Ser Val Pro<br>755  |                | Pro Gl        | u Leu<br>760 |            | Leu        | Tyr        | Ser        | Leu<br>765  | Val         | Phe        | Val        |
| Leu Phe Cys<br>770  | Asp Glu        | Val Ax        | -            | Trp        | Tyr        | Val        | Asn<br>780 | Gly         | Val         | Asn        | Tyr        |
| Phe Thr Asp         | Leu Trp        | Asn Va        | ıl Met       | Asp        | Thr        | Leu<br>795 | Gly        | Leu         | Phe         | Tyr        | Phe<br>800 |
| Ile Ala Gly         | Ile Val<br>805 |               | g Leu        | His        | Ser<br>810 | Ser        | Asn        | Lys         | Ser         | Ser<br>815 | Leu        |
| Tyr Ser Gly         | Arg Val<br>820 | Ile Ph        | e Cys        | Leu<br>825 | Asp        | Tyr        | Ile        | Ile         | Phe<br>830  | Thr        | Leu        |
| Arg Leu Ile<br>835  |                | Phe Th        | r Val<br>840 | Ser        | Arg        | Asn        | Leu        | Gly<br>845  | Pro         | Lys        | Ile        |
| Ile Met Leu<br>850  | Gln Arg        | Met Le        |              | Asp        | Val        | Phe        | Phe<br>860 | Phe         | Leu         | Phe        | Leu .      |
| Phe Ala Xaa<br>865  | Trp Met        | Val Al<br>870 | a Phe        | Gly        | Val        | Ala<br>875 | Arg        | Gln         | Gly         | Ile        | Leu<br>880 |
| Arg Gln Asn         | Glu Gln<br>885 |               | p Arg        | Trp        | 11e<br>890 | Phe        | Arg        | Ser         | <b>Val</b>  | Ile<br>895 | Tyr        |
| Glu Pro Tyr         | Leu Ala<br>900 | Met Ph        | e Gly        | Gln<br>905 | Val        | Pro        | Ser        | Asp         | Val<br>910  | Asp        | Gly        |
| Thr Thr Tyr<br>915  | Asp Phe        | Ala Hi        | s Cys<br>920 | Thr        | Phe        | Thr        | Gly        | Asn<br>925  | Glu         | Ser        | Lys        |
| Pro Leu Cys<br>930  | Val Glu        | Leu As        | 7.           | His        | Asn        | Leu        | Pro<br>940 | Arg         | Phe         | Pro        | Glu        |
| Trp Ile Thr<br>945  | Ile Pro        | Leu Va<br>950 | l Cys        | Ile        | Tyr        | Met<br>955 | Leu        | Ser         | Thr         | Asn        | 960        |
| Leu Leu Val         | Asn Leu<br>965 | Leu Va        |              | Met        | 970        |            |            |             |             | 975        |            |
| Val Gln Glu         | Asn Asn<br>980 | Asp Gl        |              |            |            |            |            |             |             |            |            |
| Val Gln Glu<br>995  | Tyr Cys        | Ser Ar        | g Leu<br>100 |            | Ile        | Pro        | Phe        | Pro<br>1005 |             | Ile        |            |
| Phe Ala Tyr<br>1010 | Phe Tyr        |               |              | Lys        |            |            |            |             | Cys         | Cys        | Cys        |
| Lys Glu Lys         | Asn Met        | Glu Se        | r Ser        | Val        | Cys        | Cys        | Phe        | Lys         | Asn         | Glu        | Asp        |

| 1025                    | •                        | . ,          |          | 103               | 0                                     |                | •                                         | 1            | 103                | 5             |                     |                      |            | 1040           |                         |
|-------------------------|--------------------------|--------------|----------|-------------------|---------------------------------------|----------------|-------------------------------------------|--------------|--------------------|---------------|---------------------|----------------------|------------|----------------|-------------------------|
| Asn G                   | lu Th                    | r Leu        |          | Trp               |                                       | Gly            |                                           | 105          | 0                  |               | Asn                 |                      | Leu<br>105 |                |                         |
| Lys I                   | le Ası                   | n Thr<br>106 | Lys<br>0 | Ala               | Asn                                   | Asp            | Thr<br>106                                | Ser          | Glu                | Glu           |                     | Arg<br>107           |            | Arg            | •                       |
| Phe A                   | rg Gl                    | 75           | _        |                   |                                       | 108            | Asn<br>0                                  | Asp          | Leu                | Lys           | Gly<br>108          | Leu<br>5             |            | 1              | •===                    |
|                         | le Al:                   | a Asn        |          | Įle               | Lys<br>109                            | 5号 *           |                                           |              |                    |               | 7. 1                |                      |            |                |                         |
|                         | •                        |              | 27 19 4  | 1.                | r př                                  | ۴.             | 1 3 3 3 4 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 | St. I        | Vari               | Poly          | 1 <u>\$</u> .7      | 3000<br>3000<br>3000 | 1.         |                | z(A)/z                  |
| <210><211><211>         |                          |              | er er    | . •               | 2 <u>12</u> 1.                        | .4.4           | •;                                        | 0.08<br>0.18 | 6 ( ).             | أباد فير      | */\$.               | er Del<br>S          | 1:5        | 1.2            |                         |
| <213>                   | Homo                     | sapi         | ens      | :                 |                                       | **             |                                           |              | 19.<br>39.         | 11,11         |                     | -41                  |            | 4.7<br>95.2    | i i                     |
| <400><br>Arg M          | 638<br>let Pro           | o Thr        | Val<br>5 |                   | Gln                                   | Суз            | Val                                       | Asn<br>10    | Val                | Ser           | Val.                |                      | Ser<br>15  |                | # 1. <b>1</b><br>5 # 1. |
| <210><br><211><br><212> |                          | . 70         | * 3      | \$ <sub>2</sub> * | P                                     | 1.1<br>7. j.j. |                                           | . 🗸          | :                  | 7.°C          | 18.3<br>6.08        | . :                  | : f3       | 5              | ,                       |
| <213>                   | Homo                     | sapi         | ens      | r                 | ```                                   |                |                                           | ţ.           |                    | 131           |                     | 970<br>124           | deid       | .;:T           | Janes.                  |
| <400><br>agaat          | gccta                    | ccgt         | gctgo    | ca gi             | tgcgi                                 | tgaa           |                                           | gtcg         | gtgg               | tgt           | cţ                  |                      |            | a.Eg           | æ <b>45</b> ⋅           |
| <211>                   | 640<br>45<br>DNA         | ŗ,           | t        |                   | i i i i i i i i i i i i i i i i i i i | 841            |                                           |              | 75<br>2.           |               | pert.               |                      |            |                | į                       |
|                         | Homo                     | sapi         | ens      | No.               | art<br>dat                            | 1              |                                           | ţs           |                    |               |                     |                      | £°-        |                | ž                       |
| <400><br>gagcc          | aggga                    | gcca         | gatg     | gt g              | gagge                                 | ccag           | c cto                                     | etec         | gtac               | ggc           | ac.                 |                      |            |                | 45                      |
| <212>                   | 641<br>45<br>DNA<br>Homo | sapi         | ens      |                   |                                       |                | , R:                                      |              |                    |               |                     |                      |            | e i            |                         |
|                         | 641                      |              | :<br>    |                   |                                       |                |                                           | ્રેકે છે.    |                    |               |                     | ÷                    | 9          |                | ,                       |
| <210>                   |                          | aaya         | ~ 13     | ag ga             | ayee.                                 | nii            | y ycq                                     | 6.60         | geca<br>Ada<br>Ada | Ja /          | : (b)               | . "                  | ٢,,        | e ja<br>Tiga   |                         |
| <211><br><212><br><213> | DNA<br>Homo              | sapi         | ens      | · (               | 294<br>2002                           | હાર 'લે        | <del>S</del>                              | 3 L.Z.       | 1611A              | let<br>Milita | 3 ° 4               | _ 15 d               | gwj.)      | : <u>:</u> ;;; | く3章 1<br>万円2            |
| <400>                   | 642<br>gcaca             | gtcti        | tgagg    | je e              | gacca                                 | aaga           | g cca                                     | -√<br>aggga  | agcc               | ∀<br>aga      | _ay<br><b>tg</b> u≾ | .>++##               | cyt.       | •5.            | 45                      |

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| <210><br><211><br><212><br><213> | 45<br>DNA        | sapiens      |             |                                       |                |                       | , ·                                   |
|----------------------------------|------------------|--------------|-------------|---------------------------------------|----------------|-----------------------|---------------------------------------|
| <400>                            | 643              | •            |             | • • •                                 | 3.             |                       |                                       |
|                                  |                  | ggctgggcct   | gcacagtctt  | gaggccgacc                            | aagag          |                       | 45                                    |
| <210><br><211><br><212><br><213> | 42<br>DNA        | sapiens      |             | . ' '                                 |                |                       |                                       |
| <400>                            | 644              | •            | e e         |                                       | and the second |                       |                                       |
|                                  |                  | cctacaccat   | cgggctgggc  | ctgcacagtc                            | tt             |                       | 42                                    |
| <210><211><211><212><213>        | 45<br>DNA        | sapiens      |             |                                       |                |                       |                                       |
| •                                | 1.               |              |             | to recive                             | •              |                       |                                       |
| <400><br>ctatca                  |                  | cacactottt   | ccagaactcc  | tacaccatcg                            | ggctg          |                       | 45                                    |
| <210><br><211><br><212>          | 646<br>45<br>DNA | sapiens      |             | •                                     |                |                       |                                       |
| <400>                            | 646              |              | 1 th single | · · · · · · · · · · · · · · · · · · · | ·, .           | •                     | v • .                                 |
|                                  |                  | gggtgctgtc   | agccgcacac  | tgtttccaga                            | actcc          |                       | 45                                    |
| <210><br><211><br><212><br><213> | 45<br>DNA        | sapiens      |             | ·                                     | ·              |                       | · · · · · · · · · · · · · · · · · · · |
| <400>                            | 647              |              |             | •                                     |                | -                     | . S = 1 = 1, .,                       |
|                                  |                  | tggtgcatcc   | gcagtgggtg  | ctgtcagccg                            | cacac          |                       | 45                                    |
| <210><br><211>                   | _                |              |             |                                       |                |                       |                                       |
| <212>                            | DNA              | -            |             |                                       |                |                       |                                       |
| <213>                            | Homo             | sapiens      |             |                                       |                |                       | 30 V.                                 |
| <400><br>aacgaa                  |                  | tctgctcggg   | cgtcctggtg  | catccgcagt                            |                |                       | 45                                    |
| <210><br><211><br><212>          | 45               |              |             |                                       |                |                       |                                       |
|                                  |                  | sapiens      |             |                                       |                |                       |                                       |
| <400>                            | 649              | 7 <u>4</u> 2 |             |                                       |                | Mary Ethiopia William |                                       |
| gcacto                           | ggtca            | tggaaaacga   | attgttctgc  | tcgggcgtcc                            | rggrg          |                       | 45                                    |
| <210><br><211>                   |                  |              |             |                                       |                | •                     |                                       |

|                                    |                  |              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                        |                                         | *                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
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| <212> DNA<br><213> Homo            | sapiens          |              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | •                      |                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <400> 650<br>tcgcagccct            | ggcaggcggc       | actggtcatg   | gaaaacgaat                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | tgttctgctc             | g                                       | 51                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| <210> 651                          |                  |              | *** 1.4                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | J. C                   | : :                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <211> 45<br><212> DNA              |                  |              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | •                      |                                         | 1 2 4                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| <213> Homo <400> 651               | sapiens          |              | · · · · · · · · · · · · · · · · · · ·                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | ı                      | 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| atcagcattg                         | cttcgcagtg       | ccctaccgcg   | gggaactett                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | gcete                  |                                         | <b>45</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| <210> 652<br><211> 45<br><212> DNA |                  | 7 )<br>      | to to a section of the section of th | 1 (1997)               | To a service of                         | and the second of the second o |
| <213> Homo                         | sapiens          |              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                        |                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <400> 652                          | agtctgacac       | catccggage   | atcagcattg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                        | e in garage                             | 45                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| <210> 653                          |                  | :            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                        |                                         | The state                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| <211> 45<br><212> DNA              | •                |              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                        |                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <213> Homo                         | sapiens          |              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                        |                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <400> 653<br>atcaagttgg            | acgaatccgt       | gtccgagtct   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                        |                                         | <b>45</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| <210> 654<br><211> 45              |                  | •            | •                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | in the calling to      | 64, 75 <b>9</b> 4, 4,75                 | ភ ភេសាល្អក្នុវ<br>-                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| <212> DNA<br><213> Homo            | sapiens          |              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                        | •                                       | , , , , , , , , , , , , , , , , , , ,                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| <400> 654                          | tgctcatcaa       | attaacass    | tecatateca                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | agtet                  | ٠.;                                     | e ↓ .<br><b>45</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| <210> 655                          | cyccoaccaa       | geeggaegaa   | cooglycoog                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | - <b>ugus</b>          | *.<br>* y                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <211> 45<br><212> DNA              |                  |              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                        |                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <213> Homo                         | sapiens          |              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                        |                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <400> 655 agaccettge               | tcgctaacga       | cctcatgctc   | atcaagttgg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | acgaa                  |                                         | 45                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| <210> 656                          |                  | ř · · ›      | 1 727 31                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0.1 <sub>6</sub> 2 2 2 |                                         | . '                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| <211> 15<br><212> PRT              |                  |              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                        | •                                       | . :                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| <213> Homo                         | sapiens          |              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                        |                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <400> 656                          | y Ser Gln Me     | at Val Glu i | Ala Sar Leu                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Ser Val Ar             | onana<br>THis                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| CIU IIO GI                         | 5<br>y ser Gri M |              | 10                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | alithe editor          | 15                                      | e jak<br>Simal                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| <210> 657                          |                  |              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                        |                                         | ∴∴                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| <211> 15                           |                  | •            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                        |                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |

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<212> PRT
<213> Homo sapiens
<400> 657
Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala Ser Leu
                                      10
                  5 . . .
<210> 658
<211> 15
<212> PRT
<213> Homo sapiens
<400> 658
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met
                 \sum_{i=1}^{n} \mathbf{5}^{i}_{i+1} \cdot \mathbf{2}^{i}_{i+1} \cdot \mathbf{2}^{i}_{i+1} = \sum_{j=1}^{n} \mathbf{10}^{j}_{i+1} \cdot \mathbf{2}^{j}_{i+1} \cdot \mathbf{2}^{j}_{i+1} \cdot \mathbf{2}^{j}_{i+1}
<210> 659
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<213> Homo sapiens
<400> 659
Tyr Thr Ile Gly Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu
                  5 10 15
<210> 660
<211> 14
<212> PRT
<213> Homo sapiens
<400> 660
Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu
    5 10
<210> 661
<211> 15
<212> PRT
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<400> '661
Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
                                        10
                                                               15. And a prof. All to
<210> 662
<211> 15
<212> PRT
<213> Homo sapiens
<400> 662
His Pro Gln Trp Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser
                                        10
                  5
                                                               15
```

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<210> 663
<211> 15
<212> PRT
<213> Homo sapiens
<400> 663
Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Ala His
                                     10
<210> 664
<211> 15
<212> PRT
<213> Homo sapiens ,
               1、2019-110 大发 (AD green to 1997)
<400> 664
Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val
<210> 665
<211> 15
<212> PRT
<213> Homo sapiens
                 E Par a record of a
Ala Leu Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val
                                     10
<210> 666
<211> 17
<212> PRT
<213> Homo sapiens
<400> 666
Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu Phe Cys
Ser
<210> 667
<211> 15
<212> PRT
<213> Homo sapiens
<400> 667
Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn Ser Cys Leu
                                                          15
<210> 668
<211> 15
<212> PRT
```

<213> Homo sapiens

| <400> 668                   |                                |                 |                                              |                                          | • • • •                                                                                                                                                                                                                           |
|-----------------------------|--------------------------------|-----------------|----------------------------------------------|------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Ser Val Ser Glu Ser Asp Th  | r Ile Ar                       | g Ser Ile       | Ser Ile                                      | Ala Ser                                  |                                                                                                                                                                                                                                   |
| 5                           |                                | 10              | 501 210                                      | 15                                       |                                                                                                                                                                                                                                   |
| •                           | •                              | 10              |                                              | 10                                       |                                                                                                                                                                                                                                   |
|                             |                                |                 |                                              |                                          |                                                                                                                                                                                                                                   |
|                             |                                |                 |                                              |                                          |                                                                                                                                                                                                                                   |
| <210> 669                   |                                |                 |                                              |                                          |                                                                                                                                                                                                                                   |
| <211> 15                    |                                |                 | • •                                          |                                          |                                                                                                                                                                                                                                   |
| <211> 15<br><212> PRT       |                                |                 | 19 1 . T 3 1 1 1 1 1                         |                                          | * · · · · · · · · · · · · · · · · · · ·                                                                                                                                                                                           |
| <213> Homo sapiens          | ng garage                      | * + 1           | T 12 1 1 1 1 1 1                             | ta t |                                                                                                                                                                                                                                   |
|                             | 1.1 :                          |                 |                                              | *                                        |                                                                                                                                                                                                                                   |
| <400> 669                   |                                | 100             |                                              | · · · · · · · · · · · · · · · · · · ·    |                                                                                                                                                                                                                                   |
| Ile Lys Leu Asp Glu Ser Va  | 1. Com C1.                     |                 |                                              |                                          |                                                                                                                                                                                                                                   |
| The bys hed Asp Gid Ser va  | T DET GT                       | n ser vab       | IIII III                                     | ard per                                  |                                                                                                                                                                                                                                   |
|                             |                                | 10              |                                              |                                          |                                                                                                                                                                                                                                   |
|                             |                                |                 |                                              |                                          |                                                                                                                                                                                                                                   |
| i kan digi yata maranda ku  |                                |                 |                                              |                                          |                                                                                                                                                                                                                                   |
| <210> 670                   |                                | San San L       | 27223 32                                     | · 2                                      | . '.                                                                                                                                                                                                                              |
| <211> 15                    |                                |                 |                                              | i e region de                            |                                                                                                                                                                                                                                   |
| 2010\ ppm or 1 155 for 1501 | A Commence of the              |                 | e e pere propie                              |                                          | • • • • • • • • • • • • • • • • • • • •                                                                                                                                                                                           |
| <213> Homo saniens          | 1 P. J. 30                     |                 | the state of a                               | 5 - 3                                    |                                                                                                                                                                                                                                   |
| <213> Homo sapiens          |                                |                 |                                              |                                          | _                                                                                                                                                                                                                                 |
| <400> 670                   | and the second                 |                 | - ;;                                         |                                          |                                                                                                                                                                                                                                   |
|                             |                                |                 |                                              |                                          |                                                                                                                                                                                                                                   |
| Asn Asp Leu Met Leu Ile Ly  | s Leu As                       | b Gra ser       | var ser                                      | Giu Ser                                  |                                                                                                                                                                                                                                   |
| 5                           |                                | 10              |                                              | 15                                       |                                                                                                                                                                                                                                   |
|                             |                                |                 |                                              |                                          | i i i i i i i i i i i i i i i i i i i                                                                                                                                                                                             |
|                             |                                | D 1 .           |                                              | 7 1 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2  | e internation                                                                                                                                                                                                                     |
| <210> 671                   |                                |                 | TOUR FOR THE                                 | (3 T 334 - 47                            |                                                                                                                                                                                                                                   |
| <210> 671<br><211> 15       | 1.711.7.13                     | 5.00            | $\{x\in \mathcal{R}^n_{i,j}(\mathbb{Z})=0\}$ | ng diti di kara                          | and the second second                                                                                                                                                                                                             |
| <211> 15                    | 2.0                            |                 | " ÷ .                                        |                                          | ٠.,                                                                                                                                                                                                                               |
| <213> Homo sanians          | of Carlos                      | 4.              | 3 13th B                                     |                                          | 1000                                                                                                                                                                                                                              |
| 1 months and save ingra     |                                |                 |                                              |                                          |                                                                                                                                                                                                                                   |
| <400> 671                   | 4 4 2 2                        | A 100           |                                              |                                          |                                                                                                                                                                                                                                   |
|                             |                                |                 | <b>* *</b> '                                 | N 07                                     |                                                                                                                                                                                                                                   |
| Arg Pro Leu Leu Ala Asn As  | р теп ме                       | t ren ite       | тур теп                                      | Asp GIU                                  |                                                                                                                                                                                                                                   |
| <b>.</b>                    | · . ·                          |                 | *                                            |                                          |                                                                                                                                                                                                                                   |
|                             | . •                            | for the same    | u ·                                          |                                          | • •                                                                                                                                                                                                                               |
| <210> 672                   |                                |                 |                                              | •                                        |                                                                                                                                                                                                                                   |
| <211> 35                    | •                              | · · · · · ·     |                                              |                                          |                                                                                                                                                                                                                                   |
| <212> DNA                   | *                              | ** .*           |                                              | 2                                        |                                                                                                                                                                                                                                   |
| <213> Artificial Sequence   |                                | 9.4             | 1. Table 17 18                               |                                          |                                                                                                                                                                                                                                   |
|                             |                                | 6.2             | 1.125 46 62                                  |                                          |                                                                                                                                                                                                                                   |
| <220>                       |                                |                 |                                              |                                          |                                                                                                                                                                                                                                   |
| <223> PCR primer            |                                |                 |                                              |                                          |                                                                                                                                                                                                                                   |
| \2237 FCR primer            |                                |                 |                                              | •                                        | 1 S 1 S 1 S 1 S 1 S 1 S 1 S 1 S 1 S 1 S                                                                                                                                                                                           |
|                             |                                |                 |                                              |                                          | and the second                                                                                                                                                                                                                    |
| <400> 672                   |                                |                 |                                              |                                          |                                                                                                                                                                                                                                   |
| ggaccagcat atgaggaaca gaag  | gaatga c                       | actc            |                                              | • 1 1.5                                  | 35                                                                                                                                                                                                                                |
|                             | •                              |                 |                                              | •                                        |                                                                                                                                                                                                                                   |
|                             |                                |                 |                                              |                                          | in and the second s<br>Second second |
| <210> 673                   |                                |                 |                                              |                                          | ે લાઉં ફાઇ જાલે                                                                                                                                                                                                                   |
| <211> 29                    |                                | <u>;</u> ,      |                                              | •                                        |                                                                                                                                                                                                                                   |
| <212> DNA                   |                                |                 |                                              |                                          |                                                                                                                                                                                                                                   |
| <213> Artificial Sequence   | Mark Light 🖜                   | er e e          | A                                            | and the second of the second             | 1.E                                                                                                                                                                                                                               |
| ZETON WICHTIGHAT pedneuce   |                                |                 |                                              | •                                        |                                                                                                                                                                                                                                   |
|                             |                                | ,               |                                              |                                          |                                                                                                                                                                                                                                   |
| <220>                       |                                | , 5 - 2-4 2 - 2 | CT .                                         | - f f 3 - 1 - 185                        |                                                                                                                                                                                                                                   |
| <220> <223> PCR primer      | garan a a <del>f</del> an<br>' |                 | n Paris III.                                 | 5 2 2 3 4 3 34                           |                                                                                                                                                                                                                                   |
|                             | •                              |                 |                                              |                                          | •                                                                                                                                                                                                                                 |
| <400> 673                   |                                |                 |                                              |                                          |                                                                                                                                                                                                                                   |
| ccgctcgagt ccaccccaag cctc  | acago                          |                 | . Maria                                      |                                          | 29                                                                                                                                                                                                                                |
|                             |                                |                 |                                              | ,                                        | 29                                                                                                                                                                                                                                |
| · ·                         |                                |                 |                                              |                                          |                                                                                                                                                                                                                                   |

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<210> 674
<211> 1959
<212> DNA
<213> Homo sapiens
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atgaggaaca gaaggaatga cactctggac agcacccgga ccctgtactc cagcgcgtct 60.
cggagcacag acttgtctta cagtgaaagc gacttggtga attttattca agcaaatttt 120
aagaaacgag aatgtgtett etttaccaaa gattecaagg ecaeggagaa tgtgtgcaag 180
tgtggctatg cccagagcca gcacatggaa ggcacccaga tcaaccaaag tgagaaatgg 240
aactacaaga aacacaccaa ggaattteet accgaegeet ttggggatat teagtttgag 300
acactgggga agaaagggaa gtatatacgt ctgtcctgcg acacggacgc ggaaatcctt 360 ...
tacgagetge tgacecagea etggeacetg aaaacaceca acetggteat ttetgtgace 420
ggggggcgcca agaacttcgc cctgaagccg cgcatgcgca agatcttcag ccggctcatc 480
tacatcocca agtecaaagg tgettggatt eteaegggag geacecatta tggeetgatg 540
aagtacatcg gggaggtggt gagagataac accatcagca ggagttcaga ggagaatatt 600
gtggccattg gcatagcagc ttggggcatg gtctccaacc gggacaccct catcaggaat 660
tgcgatgctg agggctattt tttagcccag taccttatgg atgacttcac aagagatcca 720
ctgtatatcc tggacaacaa ccacacat ttgctgctcg tggacaatgg ctgtcatgga 780
catcccactg tcgaagcaaa gctccggaat cagctagaga agtatatctc tgagcgcact 840
attcaagatt ccaactatgg tggcaagatc cccattgtgt gttttgccca aggaggtgga 900
aaagagactt tgaaagccat caatacctcc atcaaaaata aaattccttg tgtggtggtg 960
gaaggctegg gecagatege tgatgtgate getageetgg tggaggtgga ggatgeeetg 1020
acatettetg eegteaagga gaagetggtg egetttttae eeegeaeggt gteeeggetg 1080
cctgaggagg agactgagag ttggatcaaa tggctcaaag aaattctcga atgttctcac 1140
ctattaacag ttattaaaat ggaagaagct ggggatgaaa ttgtgagcaa tgccatctcc 1200 🚲
tacgctctat acaaagcctt cagcaccagt gagcaagaca aggataactg gaatgggcag 1260
etgaagette tgetggagtg gaaccagetg gaettageea atgatgagat ttteaccaat 1320 mm
gaccgccgat gggagtctgc tgaccttcaa gaagtcatgt ttacggctct cataaaggac 1380
agacceaagt ttgtccgcct ctttctggag aatggcttga acctacggaa gtttctcacc 1440
catgatgtcc tcactgaact cttctccaac cacttcagca cgcttgtgta ccggaatctg 1500
cagategeca agaatteeta taatgatgee eteeteaegt ttgtetggaa actggttgeg 1560
aactteegaa gaggetteeg gaaggaagae agaaatggee gggaegagat ggaeatagaa 1620
ctccacqacq tqtctcctat tactcggcac cccctgcaag ctctcttcat ctgggccatt 1680
cttcagaata agaaggaact ctccaaagtc atttgggagc agaccagggg ctgcactctg 1740
gcagccetgg gagccagcaa gcttetgaag actetggcca aagtgaagaa cgacatcaat 1800
gctgctgggg agtccgagga gctggctaat gagtacgaga cccgggctgt tgagctgttc 1860
actgagtgtt acagcagcga tgaagacttg gcagaacagc tgctggtcta ttcctgtgaa 1920
                                                                 1959
gettggggtg gaetegagea ceaceaceae caccactga
<210> 675
<211> 652
<212> PRT
<213> Homo sapiens
<400> 675
Met Arg Asn Arg Arg Asn Asp Thr Leu Asp Ser Thr Arg Thr Leu Tyr
Ser Ser Ala Ser Arg Ser Thr Asp Leu Ser Tyr Ser Glu Ser Asp Leu
Val Asn Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe
                                                                 $70 KL 4.
Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala
    50
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| Gln<br>65 | Ser         | Gln        | His                     | Met       | Ģlu<br>70    | Gly        | Thr           | Gln           | Ile       | Asn<br>75                                | Gln        | Ser        | Glu                | ГÀЗ       | Trp<br>80  |
|-----------|-------------|------------|-------------------------|-----------|--------------|------------|---------------|---------------|-----------|------------------------------------------|------------|------------|--------------------|-----------|------------|
| Asn       | Tyr         | Lys        | Lys                     | His<br>85 |              | Lys        | Glu           | Phe           | Pro<br>90 | Thr                                      | Asp        | Ala        | Phe                | Gly<br>95 | Asp        |
| Ile       | Gln         | Phe        | Glu<br>100              | Thr       | Leu          | Gly        | Lys           | Lys<br>105    | Gly       | Lys                                      | Tyr        | Ile        | Arg<br>110         | Leu       | Ser        |
| Cys       | Asp         | Thr<br>115 | Asp                     | Ala       | Glu          | Ile        | Leu<br>120    | Tyr           | Glu       | Leu                                      | Leu        | Thr<br>125 | Gln                | His       | Trp        |
| His       | Leu<br>130. |            | Thr                     | Pro       | Asn          | Leu<br>135 | Val           | Ile           | Ser       | Val                                      | Thr<br>140 | Gly        | Gly                | Ala       | Lys        |
| 145       |             | *          | Leu                     |           | 150          |            |               | 1<br>- 1: - 1 |           | 155                                      | ,          | **         |                    |           | 160        |
| -         |             | •          |                         | 165       |              |            | : -           | • 1,          | 170       | •                                        |            |            | : "                | 175       |            |
|           |             |            | Met <sup>*</sup><br>180 |           | ;<br>;<br>-, | . 1        | 77.5          | 185           |           |                                          |            |            | 190                | ٠,        | . 44       |
|           | _           | 195        | Ser                     | *         | · .          |            | 200           | ٠.,           | .57       | ٠.                                       | : : 1      | 205,       | . • . •            | 31 -      |            |
|           | 210         |            | Ser                     | •         | 1 17         | 215        | . :: 18       | •             | į.        | 1                                        | 220        | * *.       |                    |           | 4.         |
| 225       |             |            | Leu                     |           | 230          |            |               | = .           |           | 235                                      |            | ;          |                    | :         | 240        |
|           |             |            | Leu                     | 245       | 1            |            |               | . •           | 250       |                                          | ٠.         |            | . '                | 255       |            |
|           |             |            | Gly<br>260              |           |              | ,          | . i           | 265           | :         | 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1 | 1          |            | 270                |           |            |
|           | _           | 275        |                         |           |              |            | 280           |               |           | : .                                      | , ,        | 285        | ,                  | •         | Gly        |
|           | 290         |            | Ile                     | 7         | ٠.           | 295        | ة م.<br>. • ح | . •           | . 1.      |                                          | 300        | *          | •. , ••            | •         |            |
| 305       |             | •          |                         |           | 310          |            | 47            |               | . 1 }     | 315                                      | :          | . 1        | ئى يېراد<br>ئارىخا | 24.5      | Val<br>320 |
|           |             |            | Gly                     | 325       |              |            | • .           | *, •          | 330       | •                                        |            | ;          | i                  | 335       |            |
|           |             |            | Leu<br>340              |           |              |            |               | 345           |           |                                          |            | •          | 350                |           |            |
|           |             | 355        |                         |           |              |            | 360           |               |           |                                          |            | 365        |                    |           | Trp        |
| Ile       | Lys         | Trp        | Leu                     | Lys       | Glu          | Ile        | Leu           | Glu           | Суз       | Ser                                      | His        | Leu        | Leu                | Thr       | Val        |

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| , 3           | 370        |            |            |            |              | 375        | 5            | ;          |            |            | 380        | ),    |       |            |              |
|---------------|------------|------------|------------|------------|--------------|------------|--------------|------------|------------|------------|------------|-------|-------|------------|--------------|
| 1le 1<br>385  | Lys i      | Met        | Glu        | Glu        | 1 Ala<br>390 | G13        | / Asp        | Glu        | ı Ile      | e Va1      | L' Sei     | C Asr | n Ala | a Ile      | e Ser<br>400 |
|               |            |            |            | 405        | •            |            |              | ;          | Ser<br>410 | Glu        | ı Glr      | a Asp | ٠     | 415        |              |
| Trp A         | lsn (      | Gly        | Gln<br>420 |            | Lys          |            |              | Leu<br>425 | Glu        |            |            | Gln   | 421   |            | Leu          |
| Ala A         | sn A       | Asp<br>435 | Glu        | Ile        | Phe          | Thr        | Asn<br>440   | Asp        |            | Arg        | Trp        | Glu   | Ser   | Ala        | Asp          |
| Leu G         | 1n (<br>50 | 31u        | Val        | Met        | Phe          | Thr<br>455 | Ala          | Leu        | Ile        | Lys        | Asp        | Ara   | Pro   | Lvs        | Phe state    |
| Val A<br>465  |            |            | Phe        | Leu        | Glu<br>470   | Asn        | Gly          | Leu        | Asn        | Leu<br>475 | Arg        | Lys   | Phe   | Leu        | Thr<br>480   |
| His A         | sp V       | 7al        | Leu        | Thr<br>485 | Glu          | Leu        |              | Ser        | Asn        | His        | Phe        | Ser   | Thr   | Leu<br>495 | Val          |
| Tyr A         | rg A       | Asn        | Leu<br>500 |            | Ile          |            | Lys          | Asn<br>505 | Ser        |            |            | Asp   |       |            | Leu          |
| Thr P         | he V<br>5  | al<br>15   | Trp        | <b>Lys</b> | Leu          | Val        | Ala<br>520   | Asn<br>&   | Phe        | Arg        | Arg        | Gly   | Phe   | Arg        | Lys          |
| Glu As        | sp A<br>30 | rg /       | Asn        | Gly        | Arg          | Asp<br>535 | Glu          | Met        | Asp        | Ile        | Glu<br>540 | Leu   | His   | Asp        | Val          |
| Ser Pr<br>545 | ro I       | le '       | Thr        | Arg        | His<br>550   | Pro        |              | Gln        | Ala        |            |            |       |       |            |              |
| Leu G         | ln A       | sn 1       | ГÀЗ        |            |              |            | Ser          |            | Val<br>570 | Ile        | Trp        | Glu   | Gln   | Thr<br>575 | Arg          |
| Gly Cy        |            | :          | 080        | ş 4.       | ٠,           | , f.       | 201          | 585        |            |            | . 1        |       | 590   |            |              |
| Ala Ly        |            |            | (          | 11.1       |              |            | 000          |            | ٧          | 5 -1       | (5), ≠     | CUO   |       |            |              |
| Ala As<br>61  | n G]<br>0  | lu I       | 'yr        | Glu        | Thr          | Arg        | Ala          | Val        | Glu        | Leu        | Phe        | Thr   | Glu   | Суз        | Tyr          |
| Ser Se<br>625 | r As       | sp G       | lu i       | Asp        | Leu          | Ala        |              | Gln        | Leu        | Len        | Val        | ጥህን   | Ser   | Cys        | Glu<br>640   |
| Ala Tr        | p Gl       | Y G        | ly 1       | Leu<br>645 | Glu i        | His :      | <b>His</b> 1 | His I      | His        | His .      | His        |       |       |            |              |

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                    55
Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr Gly Asp Val
                                   75
Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr Ala Met Ala
              85 ,
                                90
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                   the contract of the state of the state of
<210> 680
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                                                                                              15
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35 40 45

Phe Leu Gly Leu Gly Val Val Asp Asn Gly Asn Gly Ala Arg Val 50 55 60

Gln Arg Val Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr 65 70 75 80

Gly Asp Val Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr 85 90 95

Ala Met Ala Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser 100 105 110

Val Thr Trp Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr 115 120 125

Leu Ala Glu Gly Pro Pro Ala Glu Phe Met Ile Arg Glu Lys Phe Ala 130 135 140

His Cys Thr Val Leu Thr Ile Ala His Arg Leu Asn Thr Ile Ile Asp 145 150 155 160

Ser Asp Lys Ile Met Val Leu Asp Ser Gly Arg Leu Lys Glu Tyr Asp 165 170 175

Glu Pro Tyr Val Leu Leu Gln Asn Lys Glu Ser Leu Phe Tyr Lys Met 180 185 190

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Leu Pro Ser Asp Gly Lys Lys Met Val His Val Gln Asp Phe Thr Ala 35 40 45

Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr Leu Gln Gly Leu Ser Phe

|            | 50         |            |            |             | ** -       | 55         |            |                  |                  | €.         | 60         |             |            |            |                                           |                |     |         |
|------------|------------|------------|------------|-------------|------------|------------|------------|------------------|------------------|------------|------------|-------------|------------|------------|-------------------------------------------|----------------|-----|---------|
| Thr<br>65  | Val        | Arg        | Pro        | Gly         | Glu<br>70  | Leu        | Leu        | Ala              | Val              | Val 75     | Gly        | Pro         | Val        | Gly        | Ala<br>80                                 |                |     |         |
| Gly        | Lys        | Ser        | Ser        | Leu<br>85   | Leu        | Ser        | Ala        | <b>Val</b>       | Leu<br>90        | Glý        | Glu        | Leu         | Alâ        | Pro<br>95  | Ser                                       |                | .•  |         |
| His        | Gly        | Leu        | Val<br>100 | Ser         | Val        | His        | Gl.ÿ       | Arg<br>105       | Ile              | Ala        | Tyr        | Val         | Ser<br>110 | Gln        | Gln                                       | * *.           |     |         |
| Pro        | Trp        | Val<br>115 |            | Ser         | Gly        | Thr        | Leu<br>120 | Arg              | Ser              | Asn        | Ile        | Leu<br>125  | Phe        | СŢА        | Lys                                       | ٠.             |     |         |
| Lys        | Tyr<br>130 | Glu        | Lys        | Glu         | Arg        | Tyr<br>135 | Glu        | Lys <sup>2</sup> | Val <sup>3</sup> | Ile        | Lys<br>140 | Ala         | Cys        | Ala        | Leu                                       |                | • • | ·       |
| Lys<br>145 | Lys        | Asp        | Leu        | G1n         | Leu<br>150 | Leu        | Glu        | Asp <sup>"</sup> | Gly              | Asp<br>155 | Leu        | Thr         | Val        | 'Ile       | Gly<br>160                                |                |     |         |
| Asp        | Arg        | Gly        | Thr        | Thr:<br>165 | Leu        | Ser        | Gly        | Gly              | Gln<br>170       | Lỳs'       | Ala        | Arg         | Val        | Asn<br>175 | Leu                                       |                |     |         |
| Ala        | Arg        | Ala        | Val<br>180 | Tyr         | Gl'n       | Asp        | Ala        | Asp<br>185       | Ile              | Tyr        | Leu        | Leu         | Asp<br>190 | Asp        | Pro                                       |                |     |         |
| Leu        | Ser        | Ala<br>195 | Val        | Asp         | Ala        | Glu        | Val<br>200 | Ser              | Arg              | His        | Leu        | Phe<br>205  | Glu        | Leu        | Cys                                       |                |     |         |
| Ile        | Cys<br>210 | Gln        | Ile        | Leu         | His        | Glu<br>215 | Lys        | Ile              | Thr              | Ile        | Leu<br>220 | Val         | Thr        | His        | Glņ                                       | " <b>y</b> .   | . • |         |
| Leu<br>225 | Gln        | Tyr        | Leu        | Lys         | Ala<br>230 | Ala        | Ser        | Gln'             | 'Ile             | Leu<br>235 | Ile        | Lėu         | Lys        | Asp        | Gly<br>240                                | 14 9<br>3      | •   |         |
| Lys        | Met        | Val        | Gln        | Lys<br>245  | Gly        | Thr        | Tyr        | Thr <sup>®</sup> | Glu<br>250       | Phe        | Leu        | Lỳs         | Ser        | Glý<br>255 | Ile                                       |                |     |         |
| Asp        | Phe        | Gly        | Ser<br>260 | Leu         | Leu        | Lys        | Lys        | Asp<br>265       | Asn              | Glu        | Glu        | Ser         | Glu<br>270 | Gln        | Pro                                       |                |     |         |
| Pro        | Val        | Pro<br>275 | Gly        | Thr         | Pro        | Thr        | Leu<br>280 | Arg              | Asn              | Arg        | Thr        | Phe<br>285  | Ser        | Glu        | Ser                                       |                |     |         |
| Ser        | Val<br>290 | Trp        | Ser        | Gln         | Gln        | Ser<br>295 | Ser        | Arg              | Pro              | Ser        | Leu<br>300 | Lys         | Asp        | Gly        | Ala                                       |                |     |         |
| Leu<br>305 | Glu        | Ser        | Gln        | Asp         | Thr<br>310 | <b>Glu</b> | Asn<br>,\  | Val<br>Gál       | Pro              | Val<br>315 | Thr        | Leu         | Ser        | Glu        | Glu<br>320                                | 8.27<br>84 (   | .*  | , · · ' |
| Asn        | Arg        | Ser        | Glu        | Gly<br>325  | Lys        | Val        | Gly        | Phe              | Gln<br>330       | Ala        | Tyr        | Lys<br>Ged  | Asn        | Tyr<br>335 | Phe 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 | k <sup>o</sup> |     | :       |
| Arg        | Ala        | Gly        | Ala<br>340 | His         | Trp        | Ile        | Val        | Phe<br>345       | Ile              | Phe        | Leu        | Ile         | Leu<br>350 | Glu        | His<br>25                                 | ্তিক্স<br>জন্ম |     | **. *   |
| His        | His        | His        | His        | His         | •.         |            | e ge C     |                  |                  | · .5 + 3   | <br>       | :<br>: :::: |            | i av       |                                           |                | . , | ٠,      |

|                              | )> 68          |                  |                        | t               | 1                    | t         |           |              |           |            |                                         |                  |           |           |           |                                          |
|------------------------------|----------------|------------------|------------------------|-----------------|----------------------|-----------|-----------|--------------|-----------|------------|-----------------------------------------|------------------|-----------|-----------|-----------|------------------------------------------|
|                              | .> 96          |                  |                        |                 | 1                    |           |           |              |           |            |                                         |                  |           |           |           |                                          |
|                              | 2> PI          |                  |                        |                 |                      |           |           |              |           |            |                                         |                  |           |           |           |                                          |
| <213                         | 5> H           | omo s            | sapie                  | ens             | ٠,                   |           |           |              |           |            | -                                       |                  |           |           | •         |                                          |
| <4n(                         | )> 68          | R.A              |                        | 1               |                      |           |           |              |           |            |                                         |                  |           |           | •         |                                          |
|                              |                |                  | Arg                    | Glu<br>5        | Lys                  | Phe       | Ala       | His          | Cys<br>10 | Thr        | Val                                     | Leu              | Thr       | Ile<br>15 | Ala       |                                          |
| His                          | Arg            | Leu              | Asn<br>20              | Thr             | Ile                  | Ile       | Asp       | Ser<br>25    | Asp       | Lys        | Ile                                     | Met              | Val<br>30 | Leu       | Asp       |                                          |
| Ser                          | Gly            | Arg<br>35        | Leu                    | Lys,            | Glu                  | Tyr       | Asp<br>40 | Glu          | Pro       | Tyr        | Val                                     | Leu<br>45        | Leu       | Gln       | Asn       | •                                        |
| Lys                          | Glu<br>50      | Ser              | Leu                    | Phe             | Tyr                  | Lys<br>55 | Met       | ,<br>Val     | Gln       | Gln        | Leu<br>60                               | Gly              | Lys       | Ala       | Glu       | · · · · · · · · · · · · · · · · · · ·    |
| Ala<br>65                    | Ala            | Ala              | Leu,                   | Thr             | Glu<br>70            | Thr       | Ala       | Lys          | Gln       | Arg<br>75  | Trp                                     | Gly              | Phe       | Thr       | Met<br>80 |                                          |
| Leu                          | Ala            | Arg              | Leu                    | Val<br>85       | Ser                  | Asn       | Ser       | Leu          | Glu<br>90 | His        | His                                     | His              | His       | His<br>95 | His       | 437                                      |
| <213<br><213<br><213<br><221 | )>             | 5<br>NA<br>rtif. | icia:                  | l Sed           | quen                 | ce        |           |              |           |            |                                         |                  |           |           |           |                                          |
|                              |                | -                |                        |                 |                      |           |           |              |           |            |                                         |                  |           |           |           | : •                                      |
|                              | 0> 6           |                  |                        |                 |                      |           |           | ~ ~~         | - ~ ~     |            |                                         |                  |           |           |           | 35                                       |
| cgc                          | ccat           | ggg (            | gate                   | cggga           | ag a                 | aatt      | tgee      | c ac         | cgc       |            |                                         |                  |           |           |           | 3,                                       |
| <21                          | 0> 60<br>L> 30 | 5                |                        |                 |                      |           |           |              |           |            |                                         |                  |           |           |           | 1 (1) (1) (1) (1) (1) (1) (1) (1) (1) (1 |
|                              | 2> D1<br>3> A: |                  | icia                   | l Se            | quen                 | cė        |           |              |           |            |                                         |                  |           |           |           |                                          |
| <220<br><221                 |                | CR ro            | rime:                  | r               |                      |           |           |              |           |            |                                         |                  |           |           | 237 1     |                                          |
|                              |                | -                |                        |                 |                      | ,         |           | 4            |           |            |                                         |                  |           |           |           | *                                        |
| <400<br>cgc                  | 0> 60<br>etcg  | B6<br>agg        | gagt                   | ttga            | ga c                 | cagc      | ctgg      | c ca         | aca       | ) (1       | ا این<br>این                            | 1514.5<br>1514.5 | );; ·     |           | 3.        | 35                                       |
| -                            | -3             | , ,              |                        |                 |                      |           |           |              |           |            | 1-11 1                                  |                  |           | e e       |           | e e total                                |
| <210<br><210                 | D> 6<br>L> 3   | 87<br>8          | rigi<br>Valgo<br>Senta | Taller<br>Light | 2 2<br>3 55 \$<br>30 |           |           | 21 1<br>25 1 |           | 1,14.<br>2 |                                         |                  | မ<br>ဗေသ  |           |           |                                          |
|                              |                | :                |                        |                 |                      |           |           | 1,31         |           |            |                                         | •                |           | , to      | 3.7       | • , •                                    |
|                              | ٠,٠            | . /              | ri ma                  |                 |                      |           |           | ٠.           |           | ٠.,        | • • • • • • • • • • • • • • • • • • • • | ·                |           | ٠.        |           |                                          |

| <400> 687 gcatggacca tatgtcagcc attgagaggg tgtcagag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 38          |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |             |
| <210> 688                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |             |
| <211> 34<br><212> DNA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |             |
| <213> Artificial Sequence                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | •           |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | •           |
| <220>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |             |
| <223> PCR primer                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |             |
| <400> 688                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |             |
| ccgctcgaga ataaggaaaa tgaagacaat ccag                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 34          |
| े हैं जिल्लाको हुन्दे दे हिंदू ग्राहर कि हुन संप्रदे साल प्रदे हैं                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 1.501       |
| 1. N                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |             |
| <210> 689<br><211> 27                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |             |
| <212> DNA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 35, 1       |
| <pre>&lt;211&gt; DNA &lt;213&gt; Artificial Sequence</pre>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 20 g        |
| и                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |             |
| <220> (220)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |             |
| <223> PCR primer                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |             |
| <400> 689 (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) (100 ) | 27          |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 1997 KIN    |
| <210> 690                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |             |
| <211> 30                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | i daga biji |
| <212> DNA (212) DNA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 5054 P.50   |
| <213> Artificial Sequence                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |             |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |             |
| <220>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |             |
| <223> PCR primer                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |             |
| <400> 690                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |             |
| cccctcgagt cactatggtc tgcctcttga                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 30          |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |             |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |             |
| <210> 691                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |             |
| <211> 915                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |             |
| <212> DNA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |             |
| <213> Homo sapiens                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |             |
| <400> 691                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 4 1         |
| atgcatcacc atcaccatca cacggccgcg tccgataact tccagctgtc ccagggtggg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 60          |
| cagggattcg ccattccgat cgggcaggcg atggcgatcg cgggccagat caagcttccc                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |             |
| accetteata tegggeetae egeetteete geetteggete tegtegacaa caacegeaac                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |             |
| ggcgcacgag tecaacgegt ggtcgggage geteeggegg caagtetegg catetecace                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |             |
| ggcgacgtga teacegeggt egacggeget eegateaact eggecacege gatggeggae                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |             |
| gegettaacg ggeatcatee eggtgaegte ateteggtga eetggeaaac caagteggge                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |             |
| ggcacgcgta cagggaacgt gacattggcc gagggacccc cggccgaatt catgcacggg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |             |
| ceceaggtge tggcaegetg etcegagtgt gettgteetg cettggetge cacetetgeg<br>ggggtgegte tggagggggt ggaeeggeea ceaacettae ceagteaagg aagtggatgg                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |             |
| ggggtgegte tggagggggt ggaeeggeea eeaaeettae eeagteaagg aagtggatgg<br>ceatgtteee acageetgag tggetgeeac etgatggetg atggageaaa ggeettagga                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |             |
| aaagcagatg geeettggee etaeettttt gttagaagaa etgatgttee atgteetgea                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |             |
| acceptance that acct taccers as testances contacts at act with                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |             |

|                                                   | gccatatac<br>ccagtcctt | gg cettgeed<br>gg ggaaacga<br>tg cetcaagg | gc agccato       | ctca gga                              | ıgcaaggt                               | gtatgctgcc     | 840                                       |
|---------------------------------------------------|------------------------|-------------------------------------------|------------------|---------------------------------------|----------------------------------------|----------------|-------------------------------------------|
| <210> 692<br><211> 304<br><212> PRT<br><213> Homo | sapiens                |                                           |                  | · · · · · · · · · · · · · · · · · · · | ************************************** |                |                                           |
| <400> 692<br>Met His Hi                           | s His His<br>5         | His His Th                                | r Ala Ala<br>10  | Ser Asp                               | Asn Phe                                | Gln Leu<br>15  |                                           |
| Ser Gln Gl                                        | y Gly Gln<br>20        | Gly Phe Al                                | a Ile Pro<br>25  | Ile Gly                               | Gln Ala                                | Met Ala        |                                           |
| Ile Ala Gl<br>35                                  |                        | Lys Leu Pr<br>40                          |                  | His Ile                               | Gly Pro<br>45                          | Thr Ala        |                                           |
| Phe Leu Gl<br>50                                  | y Leu Gly              | Val Val As<br>55                          | p Asn Asn        | Gly Asr<br>60                         | Gly Ala                                | Arg Val        |                                           |
| Gln Arg Va<br>65                                  | l Val Gly              | Ser Ala Pr<br>70                          | o Ala Ala        | Ser Leu<br>75                         | Gly Ile                                | Ser Thr<br>80  |                                           |
| Gly Asp Va                                        | l Ile Thr<br>85        | Ala Val As                                | p Gly Ala<br>90  | Pro Ile                               | Asn Ser                                | Ala Thr<br>95  | ; ·                                       |
| Ala Met Al                                        | a Asp Ala<br>100       | Leu Asn Gl                                | y His His<br>105 | Pro Gly                               | Asp Val                                |                | :<br>:: ::::::::::::::::::::::::::::::::: |
| Val Thr Tr                                        | _                      | Lys Ser Gl<br>12                          |                  |                                       | Gly Asn<br>125                         | Val Thr        |                                           |
| Leu Ala Gl                                        | u Gly Pro              | Pro Ala Gl<br>135                         | u Phe Met        | His Gly                               |                                        | Val Leu        |                                           |
| Ala Arg Cy<br>145                                 | s Ser Glu              | Cys Ala Cy<br>150                         | s Pro Ala        | Leu Ala<br>155                        | Ala Thr                                | Ser Ala<br>160 |                                           |
| Gly Val Ar                                        | g Leu Glu<br>165       | Gly Val As                                | p Arg Pro<br>170 | Pro Thi                               | Leu Pro                                | Ser Gln<br>175 | 1971 - 1971<br>1971 - 1971 - 1971         |
| Gly Ser Gl                                        | y Trp Pro<br>180       | Cys Ser Hi                                | s Ser Leu<br>185 | Ser Gly                               | Cys His<br>190                         |                | e i Archiel<br>Storkerse                  |
| Ala Asp Gl                                        |                        | Ala Leu Gl<br>20                          |                  |                                       | Pro Trp<br>205                         | ;              | akina diribu.<br>Kabupatèn                |
| Leu Phe Va                                        | l Arg Arg              | Thr Asp Va<br>215                         |                  | Pro Ala                               | Ala Ser                                | · .            |                                           |
| Gly Gly Cy<br>225                                 |                        | Ser Ser Tr<br>230                         |                  | 235                                   | Glu Val                                | 240            |                                           |
| Cys Ser Le                                        | -                      | Leu Gly Le                                | u Ala Gln<br>250 | His Ala                               | Gln Ala                                |                |                                           |

| * .                     |        |                  | <b>,</b>        |                | ,              |        |           |                                             |          | -           |               |           |                    |                  | ٠.                                    |       |
|-------------------------|--------|------------------|-----------------|----------------|----------------|--------|-----------|---------------------------------------------|----------|-------------|---------------|-----------|--------------------|------------------|---------------------------------------|-------|
| Leu Leu Leu             | Cys    | Tyr,             | ŗys             | Trp            | Ser            | His    | Ile       | Gly                                         | Glu      | Thr         | Ser           | Ser       | His                |                  |                                       |       |
|                         | 260    |                  |                 | :              |                | 265    | An Dia    | 1.5                                         | 13 34    | • .         | 270           | ٠.        | Ş .                | ٠                |                                       |       |
| Leu Arg Ser             | Lvs    | Val.             | Tvr             | Ala            | Ala            | Phe    | Glv       | Glv                                         | Ser      | Ser         | Pro           | Cvs       | Leu                | • •              | -                                     |       |
| 275                     | _      |                  | -1-             |                | 280            |        |           | 4                                           |          | 285         |               |           |                    | 5                |                                       |       |
|                         |        | _ ′              | _               |                | :              | ~      |           | _                                           | _        | _           | <b>~</b> 1    | •         | <u>.</u>           | r                | · .                                   |       |
| Lys Gly Leu<br>290      | Met    | Ser              | Leu             | Trp 295        |                | Ser    | Trp       | Leu                                         | Ser      |             | GTĀ           |           | Pro                |                  | · · · · · · · · · · · · · · · · · · · |       |
| 290                     |        |                  | *               | 233            | ż              |        | 1         |                                             |          |             | ÷             |           |                    | •                |                                       | •     |
|                         |        |                  |                 |                |                |        | 1         | 1                                           |          | : 1         |               |           |                    | • :              | V -                                   | , , i |
| <210> 693               |        | . '              | 11.2            | 1 2 3          | 15 3.          |        |           | . :                                         | 1,4      | • ••        | 2′ ≥          |           | i                  | ₹ 1.77           | 3 A                                   |       |
| <211> 24                |        | , i              |                 | i .            |                |        | . 3.1     |                                             |          |             |               |           |                    |                  |                                       |       |
| <212> DNA               |        | 1 1 1            | La Constitution | ais            |                | ÷13.   | C.12      | MIL                                         | 41 £ 5½  | Pne.        | _1 i          |           |                    | $\Delta^* \cong$ |                                       |       |
| <213> Artif:            | icial  | L Se             | dnev            | ce             |                | 1      |           | 6.8                                         |          |             |               |           | 1/3                |                  |                                       |       |
| <220>                   |        |                  |                 | ,              | e ( )          | 54 54. | e(*)      | ত রাজ                                       | <b>(</b> | na E        |               | g 1       | ٠,                 | · . v            | e c                                   |       |
| <223> PCR p             | rimer  | 2                |                 | r, ·           |                |        |           |                                             | 2.       | , .         |               |           |                    | . !              |                                       |       |
| 4400> 600               | Þ      |                  |                 |                |                |        |           |                                             | ı        |             |               |           |                    |                  |                                       | 1     |
| <400> 693 cgaagtcacg    | tagaa  | igee.            | .⊹.<br>aorco    | etc            | Ĺ              | ,      |           | 4.11                                        | 5 1.5    | , <i>''</i> | ÷ ,           | •         | , s <sub>2</sub> , | 24               |                                       |       |
|                         |        |                  |                 |                |                |        |           |                                             |          | •           |               |           |                    |                  |                                       |       |
| 1010) 604               |        | ~t · ~           | V. 7            | 112            | * 1            | ુ      | . ,       | ÷ .,                                        | ٧٠ ،     | £ 1.1       |               | Ž         |                    | }                |                                       | -     |
| <210> 694<br><211> 29   | Δ.     |                  |                 |                |                | ~'     |           |                                             |          |             | : "           |           |                    |                  |                                       |       |
| <212> DNA               |        | 1.4.5            | a P             |                | . 57           | ,      | لم الدار  |                                             | 12.41    |             | - 1           |           | : 31               |                  |                                       |       |
| <213> Artif:            | icial  | L Sec            | quen            | ce             |                |        | i* `      |                                             |          |             |               | 2.        |                    |                  |                                       |       |
| <220>                   |        |                  |                 |                |                | ,      |           |                                             | . 7.3    | , ;         | . ,. 7        | n. 11. 1  | 73).               | 6.5              | 64                                    | Ξ,    |
| <223> PCR p             | rimeı  | <b>.</b> \       | 1262 (          | ,              |                | -      |           | 2 .                                         |          |             |               | *****     |                    | **               | ·                                     |       |
|                         |        |                  |                 |                |                |        |           |                                             |          |             |               |           |                    |                  |                                       |       |
| <400> 694<br>cctgaccgaa | ttcat  | taad             | st. or          | rect           | ggac           | ÷ -,   |           | 1.0                                         | r        |             |               |           | ٠.                 | 29               |                                       |       |
| ootgaoogaa              |        |                  | J- 9;           | 1              | <b>J</b> J – - |        | •         |                                             |          |             |               |           |                    | •                |                                       |       |
| .0.0                    | ; ·,   | . 17             |                 | و دري          | ,/             |        | ,         |                                             | ٠.       | . 4         |               |           |                    |                  |                                       |       |
| <210> 695<br><211> 166  |        |                  |                 |                |                |        |           |                                             |          |             |               |           |                    |                  |                                       |       |
| <212> PRT               | V 10.2 |                  | · 1.            | <del>.</del> - | . s.î.         |        | a         |                                             | e de     | · r         | . ,           | ,         |                    |                  |                                       |       |
| <213> Homo              | sapie  | ens              |                 |                |                | 3      |           |                                             | _        |             |               |           |                    |                  |                                       |       |
| <220>                   |        |                  |                 |                | ÷              |        | ٠         |                                             |          |             |               | ì         |                    |                  |                                       |       |
| <221> VARIA             | NT     | - 34 7<br>- 63 4 |                 | . 1.           | <b>.</b>       |        | 1115      | . ;                                         |          |             |               | -         |                    |                  |                                       | •     |
| <222> (1)               |        |                  |                 |                |                |        |           |                                             |          |             |               |           |                    |                  |                                       |       |
| <223> Xaa =             | Any    | Amıı             |                 |                | V.L            |        | 7.10      | 1 10<br>1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 |          | •           |               | ,         | <u> </u>           | · 17             |                                       | ·     |
| <400> 695               |        |                  |                 |                |                |        |           |                                             |          |             |               |           |                    |                  | •                                     |       |
| Met Gly His             | His    | His              | His             | His            | Hiş,           | Val    |           | Ala                                         | Ser      | Leu         | Ser           |           | Arg                |                  |                                       |       |
| 1<br>His Pro Glu        | Tvr    | Asn              | Ara             | Pro            | Lev            | Leu    | 10<br>Ala | Asn                                         | Asp      | Leu         | Met           | 15<br>Leu | Ile                | 68.1             |                                       |       |
|                         | 20     | ,                |                 |                |                | 25 .   | 5 ev.     | ) - 25°                                     |          | رف د د      | 30            |           | 6 999              | e gar            |                                       | ι.    |
| Lys Leu Asp             | Glu    | Ser              | Val             | Ser            | Glu            | Ser    | Asp       | Thr                                         | Ile      | Arg         | Ser           | Ile       | Ser                |                  |                                       | ٠.    |
| 35<br>Ile Ala Ser       | Gln    | Cve              | Pro-            | .ሞኮተ           | 40<br>Ala      | G) v   | Asn       | Ser                                         | Cvs      | 45<br>Leu   | o <b>Va</b> l | Ser       | Glv                |                  | , ,                                   | ٠,    |
| 50                      |        |                  |                 | 55             |                | 4.7    |           | ٠.                                          | 60       |             | ೧೯            | Ţ         |                    | 1 m. V.          | . (                                   | •     |
| Trp Gly Leu             | Leu    | Ala              |                 |                |                |        |           |                                             |          |             |               |           |                    |                  |                                       |       |
| 65<br>Asn Val Ser       | 17a1   | val              | 70 ·            | Glin           | Glin           | Val.   | Cure      | 975 €<br>Ser                                | ) asia   | T.em        | i be<br>Tur   | Asn       | Bro                | • •              | . •                                   |       |
| Wall Aut 961            | Val    | AGT              | PET             | JIU            | J_U            | AGT    | Cys       | ∵ne <sub>T</sub>                            | пÃэ      | cu          | - X -         | باست      |                    |                  |                                       |       |

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85
                                   90
                                                      95
Leu Tyr His Pro Ser Met Phe Cys Ala Gly Gly Gln Xaa Gln Xaa
                              105
Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro Leu Ile Cys Asn Gly Tyr
                          120
       115
                                              125
Leu Gln Gly Leu Val Ser Phe Gly Lys Ala Pro Cys Gly Gln Val Gly
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Lys Thr Val Gln Ala Ser
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                 5
 Gly Glu Ala Lys Ala Glu Gly Ala Ala Pro Pro Thr Pro Ser Lys Pro
                                     47.3
                                 25
                                            - 의 대한 기사인 30년 - 1만
 Leu Thr Ser Phe Leu Ile Gln Asp Ile Leu Arg Asp Gly Ala Gln Arg
                                                 45 · 05 5
 Gln Gly Gly Arg Thr Ser Ser Gln Arg Gln Arg Asp Pro Glu Pro Glu
 Pro Glu Pro Glu Gly Gly Arg Ser Arg Ala Gly Ala Gln Asn
                                         75
 Asp Gln Leu Ser Thr Gly Pro Arg Ala Ala Pro Glu Glu Ala Glu Thr
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 Leu Ala Glu Thr Glu Pro Glu Arg His Leu Gly Ser Tyr Leu Leu Asp
                                 105
                                                     110
 Ser Glu Asn Thr Ser Gly Ala Leu Pro Arg Leu Pro Gln Thr Pro Lys
                                                           455
                             120
                                                 125
 Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln Val Ile
    130
                         135
                                             140
Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala Pro Glu 145 150 150 160
                                        155 * ******** ** ** 160.
Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln Val Lys 165 170 175
Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln Leu Ser
180
Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala Leu Lys
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atectgeggg acggegegea geggeaagge ggeegeaega geagecagag acagegegae
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gaccagetga geacegggee eegegeegeg eeggatgagg eegagaeget ggeagagaee
                                                                    77 300 s
gagccagaaa ggcacttggg gtcttatctg ttggactctg aaaacacttc aggcgccctt 300 360
ccaaggette eccaaaceee taageageeg cagaageget eccgagetge etteteceae
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                                                                      480
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Gly Ala Arg Trp Pro His Thr Gly Lys Arg Gly Pro Leu Leu Gln Gly
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           20
Leu Thr Trp Ala Thr Gly Gly His Cys Phe Ser Ser Glu Glu Ser Gly
                                             45
Ala Val Asp Gly Ala Gly Gln Lys Lys Asp Arg Ala Trp Leu Arg Cys
                                         60
                       55
Pro Glu Ala Val Ala Gly Phe Pro Leu Gly Ser Asp Cys Arg Glu Gly
                                     75
                   70
Gly Arg Gln Gly Cys Gly Gly Ser Asp Asp Glu Asp Asp Leu Gly Val
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                                  90
               85
Ala Pro Gly Leu Ala Pro Ala Trp Ala Leu Thr Gln Pro Pro Ser Gln
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           100
Ser Pro Gly Pro Gln Ser Leu Pro Ser Thr Pro Ser Ser Ile Trp Pro
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        115
Gln Trp Val Ile Leu Ile Thr Glu Leu Thr Ile Pro Ser Pro Ala His
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Glu
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                                               | g gecetectg<br>c aggagetgtg<br>c tgtegetgge<br>g gagtgaegat<br>c ceagectece<br>g gecteagtgg | cagggectea ce<br>gatggtgetg ga<br>ttecetttgg ga<br>gaggatgace tg<br>teacagtete et<br>gteattetga te                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | tgggccac agga cagaagaa ggac cagactg cagg gggtggc tcca ggccctca gtct actgaact gacc | ggacac       120         agggcc       180         gaggga       240         ggcctt       300         ctcccc       360         ataccc       420                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          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| <210> 705<br><211> 132<br><212> PRT<br><213> Homo sapiens                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | !                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 97 - <b>0</b> 3                                                                   | in the second of |
| <400> 705<br>Thr Ala Ala Ser Asp A                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | sn Phe Gln L                                                                                | eu Ser Gln Gl                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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| Ala Ile Pro Ile Gly G                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  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| Gly Gly Gly Ser Pro T                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | hr Val His I<br>40                                                                          | le Gly Pro Th                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | r Ala Phe Leu<br>45                                                               | Gly                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    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| Leu Gly Val Val Asp A                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                             | sn Gly Ala Aro                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            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| Val Gly Ser Ala Pro A                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  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| 65 7 Ile Thr Ala Val Asp G                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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| Asp Ala Leu Asn Gly H                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  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| <b>100</b> ) m                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                             | 05 A S. V.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 110                                                                               | •                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Gln Thr Lys Ser Gly G                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  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                                                                                                                                                                                            | 1 Thr Leu Ala                                                                     | Giu<br>I M I                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           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| Gly Pro Pro Ala<br>130                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | i Tile<br>Herrey Willest Allender<br>Herrey                                                 | w W W est                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | ij<br>Postava postava ij                                                          | A Tool of                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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| <210> 706                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | A War Commence                                                                              | All the state of t | \$                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <211> 31                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | end the visit                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           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| <212> DNA 300 CO CONTROL SEQUENTIAL SEQUENTI | ence <sub>s for th</sub> is.                                                                | ing the second of the second o | eg ·                                                                              | · · · · · · · · · · · · · · · · · · ·                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
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| <223> PCR primer                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 7.4                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           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                                                                                                                                                                                                                                                                                                                               |
| <400> 706                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | ر ۱۳۰۰ کا فیور الجهری<br>از فر                                                              | e i didd seit e                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | න්ගි කුණා කියම ලක<br>පතුර                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| ggggaattca tcacctatgt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | gccgcctctg                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Dar of St. 1.<br>Se                                                               | ng - 1 ( <b>31</b> : <sup>3</sup> )                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| <210> 707<br><211> 40<br><212> DNA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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                                                                                                                                                                                                                                                                                                                               |
| <213> Artificial Sequ                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  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                                                                                                                                                                                            |                                                                                   | Section 1999<br>Liberary                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               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| <220><br><223> PCR primer                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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                                                                                                                                                                                            | 3                                                                                 | ustudi.<br>Kapidini alimba ili salah salah                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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                                    25
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              Gln Arg Val Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr
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Gly Asp Val Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr
                                        90
Ala Met Ala Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser
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בו בפנפסום אות הובופספם ו -

|         | 1          |            |            | 100        |            |            |            |            | 105        |                    |            |              |                | 110        |            | •          | •                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|---------|------------|------------|------------|------------|------------|------------|------------|------------|------------|--------------------|------------|--------------|----------------|------------|------------|------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1       | Val        | Thr        | Trp<br>115 | Gln        | Thr        | Lys        | Ser        | Gly<br>120 | Gly        | Thr                | Arg:       | Thr          | Gly<br>125     | Asn        | Val        | Thr        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|         | Leu        | Ala<br>130 | Glu        | Gly        | Pro        | Pro        | Ala<br>135 | Glu        | Phe        | Ile                | Thr        | Tyr<br>140   | Val            | Pro        | Pro        | Leu        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|         | Leu<br>145 | Leu        | Glu        | Val        | Gly        | Val<br>150 | <b>Glu</b> | Glu        | Lys        | Phe                | Met<br>155 | Thr          | Met            | Val        | Leu        | Gly<br>160 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|         | Ile        | Gly        | . i a .    |            | 165        |            |            | 2.22       | pi ile     | Val<br>170         | .15        | ٠<br>٠٠٠     | arije,         | 7          | 175        | Ala        | Looper Lin<br>The Art Lingson<br>Artist Suint                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| )<br>): | Ser        | Asp        | His        | Trp        | Arg-       | Gly        | Arg        | Tyr        | Gly<br>185 | Arg                | Arg        | Arg          | Pro            | Phe<br>190 | Ile        | Trp        | in againt in again<br>La kiji againi                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|         | Ala        | Leu        | Ser<br>195 |            | Gly        | Ile        | Leu        | Leu        | Ser        | Leu                | Phe        | Leu          | Ile            | Pro        | Arg        | Ala        | នៅមួយប្រជាជា<br>សហមន្តការប្រជុំប្រ                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|         | Gly        | "          | Leu        | Ala        | Gly        |            | Leu<br>215 | Cys        | Pro        | Asp                |            |              |                |            | Glu        | Leu        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|         | Ala<br>225 | Leu        |            |            |            |            |            |            |            | Leu                | 235        | િક્ષ્        | e<br>Service   | . 7        | Gln        | 240        | made et al.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|         | Суз        | Phe        | Thr        |            | Leu<br>245 |            |            |            |            | Ser<br>250         | Asp        | Ley<br>કુકુક | ь <u>у</u> сь. | Arg        | 255        | Pro        | ou service of a se |
|         | Asp        | His        | Суз        | Arg<br>260 |            | Ala        | Tyr        | Ser        |            | Tyr                | Ala        | Phe          | Met            | Ile        | Ser        | Leu<br>Leu | ් වැන්නේ ප්රක්ෂය<br>කොහැන් ස්වියක්<br>කොහැන්නේ වැන්නේ                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
|         | Gly        | Gly        | Cys<br>275 | Leu        | Gly        | Tyr        | Leu        | Leu<br>280 | Pro        | Ala                | Ile        | Asp          | Trp<br>285     | Asp        | Thr        | Ser        | •                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|         | Ala        | Leu<br>290 | Ala        | Pro        | Tyr        | Leu        | Gly<br>295 | Thr        | Gln        | G1u                | Glu        | Суз<br>300   | Leu            | Phe        |            | Leu        | 1.2 (1.2)<br>1.2 (1.3)<br>2.3 (1.3)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|         | Leu<br>305 | Thr        | Leu        | Ile        | Phe        | Leu<br>310 | Thr        |            | Val        | Ala<br>:           |            |              | Leu            |            |            |            | g v                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|         | Glu        | Glu        | Ala        | Ala        |            |            |            |            |            | Pro<br>330         |            |              |                |            | Ser<br>335 | Ala        | 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|         | Pro        | Ser        | Leu        |            |            |            |            |            |            | Cys<br>≀⊴          |            |              |                |            |            |            | *)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|         | Arg        | Asn        |            |            |            |            |            |            |            | Leu<br>coa         |            |              |                |            |            | Arg        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|         | Met        | Pro<br>370 | _          |            |            | _          | _          |            |            | <b>Val</b><br>.127 |            |              |                |            |            | _          | JAM COLOR                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|         | Met<br>385 | Ala        | Leu        |            |            |            |            |            |            | Tyr<br>* A         |            |              |                |            |            |            | Mark of State of Stat |
|         |            |            |            |            | ٠. ,       |            |            |            |            | 7.0                |            |              |                |            | 415        |            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |

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មិស្តី ដែលស៊ី ស្តីមិនស៊ី ដែល នៃជា សំពីទី ដែលស្គាល់មុខ ខែជា ១០១៦ ១៤
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Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met
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| Lys               | Pro        | Arg        | Arg<br>20  | Asn        | Leu        | Glu        | Glu                  | Asp<br>25  | Asp       | Tyr        | Leu          | His        | Lys<br>30  | Asp        | Thr                  | •                                     |
|-------------------|------------|------------|------------|------------|------------|------------|----------------------|------------|-----------|------------|--------------|------------|------------|------------|----------------------|---------------------------------------|
| Gly               | Glu        | Thr<br>35  | Ser        | Met        | Leu        | Lys        | Arg<br>40            | Pro        | Val       | Leu        | Leu          | His<br>45  | Leu        | His        | Gln                  |                                       |
| Thr               | Ala<br>50  | His        | Ala        | Asp        | Glu        | Phe<br>55  | Asp                  | Cys        | Pro       | Ser        | Glu<br>60    |            | Gln        | His        | Thr                  | :                                     |
| Gln<br>65         | Glu        | Leu        | Phe        | Pro        | Gln<br>70  | Trp        | His                  | Leu        | Pro       | 11e<br>75  | _            |            |            | Ala        | Ile<br>80            |                                       |
| Ile               | Ala        | Ser        | Leu        | Thr<br>85  | Phe        | Leu        | Tyr                  | Thr        | Leu<br>90 | Leu        | Arg          | Glu        | Val        | 95         |                      |                                       |
| Pro               | Leu        | Ala        | Thr<br>100 | Ser        | His        | Gln        | Gln                  | Tyr<br>105 | Phe       |            |              |            | Pro<br>110 | Ile        | Leu                  | ·.                                    |
| Val               | Ile        | Asn<br>115 | ГÀЗ        | Val        | Leu        | Pro        | Met<br>120           | Val        | Ser       |            |              |            |            |            |                      |                                       |
| Val               | Tyr<br>130 | Leu        | Pro        | Gly        | Val        | Ile<br>135 | Ala                  | Ala        | Ile       | Val        | Gln<br>140   | Leu        | His        | Asn        | Gly                  |                                       |
| Thr<br>145        | Lys        | Tyr        | Lys        | Lys        | Phe<br>150 | Pro        | His                  | Trp        | Leu       | Asp<br>155 | Lys          | Trp        | Met        |            | Thr<br>160           |                                       |
| Arg               | Lys        | Gln        | Phe        | 165        | قد يا أ    |            | ;;;; e               |            |           |            | -4.3 f       | မသည်ခွ     | ್ ಪಡ       | 175        |                      | Tarana<br>Tarana<br>Tarana            |
| Ile               |            | ķέ         | 180        | Ser        | Tyr        | Pro        | Met                  | Arg<br>185 | Arg       | Ser        | Tyr.         | Arg        | Tyr<br>190 | Lys        | Leu                  | ាយ ខែក្រុង .                          |
| Leu               | Asn        | Trp        | Ala        |            | Gln        | Gln        | Val.<br>200          | Gln        | Gln       | Asn        | Lys          | G1u<br>205 | Asp        | Ala        | Trp                  |                                       |
| Ile               | 210        |            | Asp        | Val        | Trp        | Arg<br>215 | Met                  | Glu        | . : :     | . 52       | Val<br>220   |            |            |            | Ile                  |                                       |
| Val<br>225        | Gly        | Leu        | Ala        | Ile        | Leu<br>230 | Ala        | Leu                  | Leu        | Ala       | Val<br>235 | Thr          | Ser        | Ile        | Pro        | Ser<br>240           | 2                                     |
| Val               | Ser        | Asp        | Ser        | Leu<br>245 | Thr        | Trp        | Arg                  | Glu        | Phe 250   | His        | Tyr          | Ile        | Gln        | Ser<br>255 | Lys.                 | 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 |
| Leu               | Gly        | Ile        | Val<br>260 | Ser        | Leu        | Leu        | Leu<br>ಟಿಕಿತ         | Gly<br>265 | Thr.      | Ile        | His<br>Adda  | Ala        | Leu<br>270 |            | Phe                  |                                       |
| Ala               | Trp        | Asn<br>275 | Lys        | Trp        | Île        | Asp        | Ile<br>280           | Lys        | Gln       | Phe        | Val          | Trp<br>285 | Tyr        | Thr        | Pro                  |                                       |
| Pro               | Thr<br>290 | Phe        | Met        | Ile        | Ala        | Val<br>295 | Phe                  | Leu        | Pro       | Ile        | Val<br>300   | Val        | Leu        |            | <b>Phe</b><br>১২,,৯১ | and look<br>week died                 |
| <b>Љуз</b><br>305 | Ser        | Ile        | Leu        | Phe        | Leu<br>310 | Pro        | Cys<br>, <u>i</u> .: | Leu<br>:   | Arg       | Lys<br>315 | Lys<br>.: (1 | Ile<br>Jij | Leu<br>신년  | Lys<br>S   | Ile<br>320           | Bary Dok<br>Kalimani                  |
| Arg               | His        | Gly        | Trp        | Glu        | Asp        | Val        | Thr                  | Lys        | Ile       | Asn        | Lys          | Thr        | Glü        | Ïle        | Cys                  |                                       |

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<211> 135

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<213> Homo sapiens

<400> 741

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             Ser Ser Leu Gln Pro Leu Pro His Arg Phe Lys Gln Phe Ser Cys Leu
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    Ser Leu Pro His Ser Trp Asp His Arg Tyr Ala Pro Pro His Leu Ala
       Asn Phe Cys Ser Phe Ser Arg Asp Gly Val Ser Leu Cys Cys Ser Gly
    Ash File eys Set File Set Arg Asp Gry Val Bet Leu Gys Gys Set St. 85 95 95 Trp Ser Lys Thr Pro Gly Leu Gln Gln Ser Ala Cys Leu Gly Leu Pro 100 105
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Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
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THE WAY THE

<210> 745

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<213> Homo sapiens

<400> 745

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5 10 15

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Ser Thr Glu Gln Asp Ser Ala Ser Lys Thr Asn Lys 65 70 75

<210> 746

<211> 80

<212> PRT

<213> Homo sapiens

<400> 746

Met Leu Leu His Ser Ser Leu Val Asn Arg Ala Arg Leu Cys Leu Lys

| 1         | ŧ                       |           |           | 5        |             |                  |           |           | 10        | -; :      |              |             |           | 15              |           |                     |                      |
|-----------|-------------------------|-----------|-----------|----------|-------------|------------------|-----------|-----------|-----------|-----------|--------------|-------------|-----------|-----------------|-----------|---------------------|----------------------|
| Asn       | Lys                     | Gln       | Ile<br>20 | Asn      | Lys         | Gln              | Thr       | Asn<br>25 | Lys       | Thr       | Glu          | Arg         | Phe<br>30 | Суз             | Cys       |                     |                      |
| Asn       | Val                     | Gln<br>35 | Gly       | Ala      | Ile         | Cys              | Ser<br>40 | Phe       | Lys       | Lys       | Ile          | Tle<br>45   | Phe       | Gly             | Gln       | •                   | -,                   |
| Ala       | Gln<br>50               | Trp       | Leu       | Thr      | Pro         | <b>Val</b><br>55 | Ile       | Pro       | Ala       | Leu       | Trp<br>60    | <b>Gl</b> u | Ala       | Lys             | Val       | •                   |                      |
| Gly<br>65 | Gly                     | Ser       | Phe       | Glu      | Val<br>70   | Arg              | Ser       | Leu       | Arg       | Ser<br>75 | Ala          | Trp         | Pro       | Thr             | Trp<br>80 | •                   | ·                    |
|           | ►<br>0> 74              |           | • :       |          | . : ,       |                  | ,1, 1     | e Tr      | O.E.      | £16.      | V '          | T-Def       | € 71.5    | : . I           | urif.     | • .                 |                      |
| <212      | l> 72<br>2> PF<br>3> Ho | T         | sapie     | ens      | E. D.       | ,,,1             | = "       |           | ent '     | 949<br>83 | , : <u>A</u> | ş T         | V 7       | .;;;;; <b>*</b> | 0;* ;     |                     |                      |
| <400      | )> 74                   | 17        |           |          | <b>√</b> c∫ | . e              | e         | *         | £1.0      | 4:"       |              | •           |           | , r. 5          | Ti e      | ,                   |                      |
| Met       | His                     | Tyr       | His       | Lys<br>5 | Asn         | Ser              | Met       | GJÀ       | Lys<br>10 | Ile       | Pro          | Pro         | His       | Asn<br>15       | Pro       | 1°<br>5.94          |                      |
| Ile       | Thr                     | Ser       | His<br>20 | Gln      | Val         | Ser              | Ser       | Asp<br>25 |           | Trp       | Asp          | Trp         | Vaļ<br>30 | Gly             | Thr       |                     |                      |
| Gln       | Ser                     | Gln<br>35 | Thr       | Val      | Ser         | Asp              | Ala<br>40 | Ala       | Gly       | Ala       | Gly          | Asp<br>45   | Thr       | Glu             | Thr       | 95                  | * * :                |
| Thr       | Gln<br>50               | Thr       | Trp       | Cys      | Leu         | Cys<br>55        | His       | Ser       | Ser       | Gly       | Leu<br>60    | Сув         | Leu       | Ser             | Pro       | •                   | 20 1<br>20 1<br>20 1 |
| Gly<br>65 | Pro                     | Pro       | Ser       | Pro      | Ser<br>70   | Met              | Val       |           |           |           |              | 1,1         |           | j               | Test is   |                     |                      |
| <211      | )> 74<br>l> 77<br>2> PI | 7         | ,         | . •      | f.o         | •.               | -72       | ŗ.        |           | ,         |              |             | Ī.a       |                 | 5         | :                   | ; ·                  |
| <213      | 3> Ho                   | omo s     | sapie     | ens      | कु व        |                  | i La      |           |           | fra .     |              |             | . 4.      |                 | -         |                     |                      |
|           | )> 74<br>His            |           | His       | Lys<br>5 | Asn         |                  | Met       | Gly       |           | Ile       | Pro<br>·     | Pro<br>CVV  | Ile       | Ile<br>15       | Gln       | ÷                   | r i i                |
| Ser       | Pro                     | Pro       | Thr<br>20 | Arg      | Ser         | Pro              | Pro       | Thr<br>25 | Arg       | GLY       | Ile          | Gly         | Trp<br>30 | Gly             | His       |                     |                      |
| Arg       | Ala                     | Lys<br>35 | Pro       | Tyr      | Gln         | Met              | Leu<br>40 | Gln       | Gly       | Leu       | Gly          | Thr<br>45   | Leu       | Arg             | Pro       | ••                  | <i>i.</i>            |
| Leu       | Arg<br>50               | Pro       | Gly       | Val      | Ser         | Val<br>55        | Thr       | Leu       | Leu       | Gly       | Ser<br>60    | Val         | Cys       |                 | Gln       | ر<br>ارا<br>اندان . | •                    |
| Asp<br>65 | Leu                     | Pro       | Pro       | Leu      | Pro<br>70   | Trp              | Tyr       | Arg       | Arg       | 75        |              |             | এএক       | W.13            | 3.7       | 2007.<br>12 14      | ·                    |

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                         5 10 15
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20 25 30
Ser Cyş Arg Asn Gly Leu Ala Ser Lys Trp Arg Gln Ala Asp Pro Ser
35
40
45
Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu Leu Phe
           50 55 60 60
              e San Springer (1997) in the contract of the c
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            10 15
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 Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
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 ctttgaactc agggtcacca ccagctattg gaccttacta tgaaaaccat ggataccaac 120
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                     20
Val Pro Thr Val Tyr Glu Val His Pro Ala Gln Tyr Tyr Pro Ser Pro
                                                 40
Val Pro Gln Tyr Ala Pro Arg Val Leu Thr Gln Ala Ser Asn Pro Val 50 to gg togonogs one 550 topo togonogs one 550 topo togonog to the case of the control of t
Tiko dga oo d
Thr Lys Lys Alas Leu Cys Iles Thr Leu Thr Leu Gly Thr Phe Leu Val
Gly Ala Ala Leu Ala Ala Gly Leu Trp Lys Phe Met Gly Ser Lys
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|            |            |            | 100        |            |                   |            |            | 105        |                   |            | ng gara    |            | 110        |            |            |
|------------|------------|------------|------------|------------|-------------------|------------|------------|------------|-------------------|------------|------------|------------|------------|------------|------------|
| ,Cys       | Ser        | Asn<br>115 | Ser        | GЉ         | Ile               | Glu        | Cys<br>120 | Asp        | Ser               | Ser        | Gly        | Thr<br>125 | Cys        | Ile        | Asn        |
| Pro        | Ser<br>130 | Asn        | Trp        | Cys        | Asp               | Gly<br>135 | Val        | Ser        | His               | Cys        | Pro<br>140 | Gly        | Gly        | Glu        | Asp        |
| Glu<br>145 | Asn        | Arg        | Cys        | Val        | Arg<br>150        | Leu        | Tyr        | Gly        | Pro               | Asn<br>155 | Phe        | Ile        | Leu        | Gln        | Met<br>160 |
| Tyr        | Ser        | Ser        | Gl'n       | Arg<br>165 | Lys               | Ser        | Trp        | His        | Pro<br>170        | Val        | Суз        | Gln        | Asp        | Asp<br>175 | Trp        |
| Asn        | Glư        | Asn        | Tyr<br>180 | Gly        | Arg               | Ala        | Ala        | Cys<br>185 | Arg               | Asp        | Met        | Gly        | Tyr<br>190 | Lys        | Asn        |
| Asn        | Phe        | Tyr<br>195 | Ser        | Ser        | Gln               | Gly        | Ile<br>200 | Val        | Asp               | Asp        | Ser        | Gly<br>205 | Ser        | Thr        | Ser        |
| Phe        | Met<br>210 | Lys        | Leu        | Asn        | Thr               | Ser<br>215 |            | Gly        | Asn               | Val        | Asp<br>220 | Ile        | Tyr        | Lys        | Lys        |
| Leu<br>225 |            | His        | Ser        | Asp        | Ala<br>230        | Cys        | Ser        | Ser        |                   | Ala<br>235 | Val        | Val        | Ser        | Leu        | Arg<br>240 |
| Cys        | Leu        | Ala        | Суз        | 245        | Val               | :          | 3          | Asn        | Ser<br>250        | Ser        | Arg        | Gln        | Ser        | Arg<br>255 | Ile        |
| Val        | Gly        | Gly        | Glu<br>260 |            | Ala               | Leu        | Pro        | Gly<br>265 | Ala               | Trp        | Pro        | Trp        | Gln<br>270 | Val        | Ser        |
| Leu        | His        | Val<br>275 |            | Asn        | Val               | His        | Val<br>280 | Cys        | Gly               | Gly        | Ser        | 11e<br>285 | Ile        | Thr        | Pro        |
| Glu        | Trp<br>290 |            | Val        | Thr        | Ala               | Ala<br>295 | His        | Cys        | Val               | Glu        | <b>Ъуз</b> | Pro        | Leu        | Asn        | Asn        |
| Pro<br>305 | _          | His        | Trp        | Thr        | <b>Ala</b><br>310 | Phe        | Ala        | Gly        | Ile               | Leu<br>315 | Arg        | Gln        | Ser        | Phe        | Met<br>320 |
| Phe        | Tyr        | Gly        | Ala        | Gly<br>325 | Tyr               | Gln        | Val        | Gln        | <b>Lys</b><br>330 | Val        | Ile        | Ser        | His        | Pro<br>335 | Asn        |
| Tyr        | Asp        | Ser        | Lys<br>340 |            |                   | Asn        |            | Asp<br>345 |                   | Ala        | Leu        | Met        | Lys<br>350 |            | Gln        |
| Lys        | Pro        |            | Thr        |            | Asn               | Asp        | Leu<br>360 |            | Lys               | Pro        | Val        | Cys<br>365 | Leu        | Pro        | Asn        |
| Pro        | Gly<br>370 |            | Met        | Leu        | Gln               | 375        | ,          | Gln        |                   |            | 1rp<br>380 | Ile        | Ser        | Gly        | Trp        |
| Gly<br>385 |            | Thr        | Glu        | Glu        | 390               | Gly        | Lys        | Thr        | Ser               | Glu<br>395 | Val        | Leu        | Asn        | Ala        | Ala<br>400 |
| Lys        | val        | Lev        | . Leu      | 11e<br>405 |                   | Thi        | Gln        | Arg        | 410               |            | Ser        | Arg        | Tyr        | Val<br>415 | Tyr        |

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Asp Asn Leu Ile Thr Pro Ala Met Ile Cys Ala Gly Phe Leu Gln Gly
                                                       425
Asn Val Asp Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Thr Ser
                                                       440
                                                                                              445
Asn Asn Asn Ile Trp Trp Leu Ile Gly Asp Thr Ser Trp Gly Ser Gly
                                    455 460
Cys Ala Lys Ala Tyr Arg Pro Gly Val Tyr Gly Asn Val Met Val Phe
                               475 (gr. 1 + ) 480
Thr Asp Trp Ile Tyr Arg Gln Met Lys Ala Asn Gly
                                485 Will you can can 490 in the AM you give but the
                          (4) An and the state of the 
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<211> 683
<212> DNA
                                                                               Professional Control of the Constitution
<213> Homo sapiens
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cggaaaaccc ctatcccgca cagcccactg tggtccccac tgtctacgag gtgcatccgg 180
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cctcaggtac ctgcatcaac ccctctaact ggtgtgatgg cgtgtcacac tgccccggcg 480
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                       20
                                                              25
Val Pro Thr Val Tyr Glu Val His Pro Ala Gln Tyr Tyr Pro Ser Pro
                                                      40
Val Pro Gin Tyr Ala Pro Arg Val Leu Thr Gin Ala Ser Asn Pro Val
Val Cys Thr Gln Pro Lys Ser Pro Ser Gly Thr Val Cys Thr Ser Lys
                                       70
                                                                              75
Thr Lys Lys Ala Leu Cys Ile Thr Leu Thr Leu Gly Thr Phe Leu Val
                                                                                                              95
```

```
Gly Ala Ala Leu Ala Ala Gly Leu Leu Trp Lys Phe M t Gly Ser Lys
                                 100 ' 105 ' 110
Cys Ser Asn Ser Gly Ile Glu Cys Asp Ser Ser Gly Thr Cys Ile Asn
115 120 125
Pro Ser Asn Trp Cys Asp Gly Val Ser His Cys Pro Gly Gly Glu Asp
                                                                                      135
Glu Asn Arg Cys Val Arg Leu Tyr Gly Pro Asn Phe Ile Leu Gln Met
145 150 155
Tyr Ser Ser Gln Arg Lys Ser Trp His Pro Val Cys Gln Asp Asp Trp
                                                         165 170
Asn Glu Asn Tyr Gly Arg Ala Ala Cys Arg Asp Met Gly Tyr Lys Asn
     180 185 190
Asn Phe Tyr Ser Ser Gln Gly Ile Val Asp Asp Ser Gly Ser Thr Ser
                         195 200
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Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly Thr
                                   5 ' 10
 Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg
                                       25
                               ्रा । १ वर्षा स्थापना वर्षे ।
१९८३ - १ वर्षा स्थापना वर्षे । १८
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 <213> Artificial Sequence
<220>
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aaatgtgaac aacatctggg tcataacgct atgtattggt acaagcaaag tgctaagaag 180 🔩
ccactggagc tcatgtttgt ctacagtctt gaagaacggg ttgaaaacaa cagtgtgcca 240
agtogottet caccigaatg coccaacage toteactiat teeticacet acaccectg 300: 😁
cagocagaag actoggooot gtatototgo gooagcagoo aagacoggac aagcagotoo 360
tacgagcagt acttegggce gggcaceagg etcaeggtea cagaggacet gaaaaacgtg 420
ttcccacccg aggtcgctgt gtttgagcca tcagaagcag agatctccca cacccaaaag 480
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| gaag<br>gcti<br>ggaa<br>cctg<br>ttca<br>acag<br>tggaa<br>gaaa | ggtcg<br>tcaca<br>acca<br>gaccg<br>accga<br>gacaa<br>agcaa<br>acctt<br>acaga | get a<br>ac t<br>ac t<br>etg o<br>att t<br>aaa o<br>aca a<br>act t | actca<br>cgggg<br>ccacc<br>ccgtc<br>ctgat<br>ctgtc<br>aatct<br>cccc | attga<br>ggack<br>ettte<br>gtace<br>etcte<br>gack<br>egack<br>ectas | aa ti      | ttcca<br>gcaal<br>acago<br>etgao<br>acaaa<br>atgao<br>gcato<br>gaaao<br>tttca | agaaq<br>tgtat<br>gcact<br>gagaq<br>atgtq<br>ggtct<br>gtgca<br>gttco | g gent to | aagaa<br>etgto<br>getaa<br>taaal<br>acaaa<br>ggacto<br>egeet<br>egeet | aaat<br>gcaa<br>aaag<br>tcca<br>agta<br>ttca<br>ttca<br>gtga | tgag<br>tggg<br>gtgg<br>aggg<br>agag<br>acag<br>acag<br>ttgg | ccaad<br>gagaq<br>acto<br>acaaq<br>acaad<br>acaga<br>aggto | ggg<br>gaa<br>gtc<br>ga<br>gag<br>gat<br>gat<br>ga | tgtca<br>cgcgg<br>tatco<br>tgtct<br>tgtgt<br>tgctg<br>tatto<br>gaaaa<br>aatco | gcaaca<br>atctcc<br>ggagga<br>cagaac<br>cgccta<br>catatc<br>gtggcc<br>ccagaa<br>agcttt | 300<br>360<br>420<br>480<br>540<br>600<br>720<br>780 | )<br>)<br>)<br>)<br>)<br>) |       |
|---------------------------------------------------------------|------------------------------------------------------------------------------|--------------------------------------------------------------------|---------------------------------------------------------------------|---------------------------------------------------------------------|------------|-------------------------------------------------------------------------------|----------------------------------------------------------------------|-----------------------------------------------|-----------------------------------------------------------------------|--------------------------------------------------------------|--------------------------------------------------------------|------------------------------------------------------------|----------------------------------------------------|-------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|------------------------------------------------------|----------------------------|-------|
| <21:                                                          | 0> 76<br>1> 31<br>2> P1<br>3> Ho                                             | L1<br>RT                                                           | sapie                                                               | ens                                                                 |            |                                                                               |                                                                      |                                               |                                                                       |                                                              |                                                              | . : .                                                      | . •                                                | ÷ *                                                                           |                                                                                        | ,                                                    |                            |       |
| <222                                                          | L> va<br>2> (3                                                               | L)                                                                 | nt<br>. (311<br>Any,                                                | L <b>)</b> ′                                                        | * .        | 1,                                                                            |                                                                      |                                               | * *                                                                   |                                                              |                                                              | •                                                          |                                                    |                                                                               |                                                                                        | : .                                                  |                            |       |
|                                                               | 0> 76<br>Gly                                                                 |                                                                    | Arg                                                                 | Leu<br>5                                                            | Xaa        | Cys                                                                           | Cys                                                                  | Ala                                           | Val                                                                   | Leu                                                          | Cys                                                          | Leu                                                        | Leu                                                | Gly<br>15                                                                     | Ala                                                                                    |                                                      | •                          | · · · |
| Val                                                           | Pro                                                                          | Met                                                                | Glu<br>20                                                           | Thr                                                                 | Gly        | Val                                                                           | Thr                                                                  | Gln<br>25                                     | Thr                                                                   | Pro                                                          | Arg                                                          | His                                                        | Leu<br>30                                          | Val                                                                           | Met                                                                                    |                                                      |                            |       |
| Gly                                                           | Met                                                                          | Thr<br>35                                                          | Asn                                                                 | Lys                                                                 | Lys        | Ser                                                                           | Leu<br>40                                                            | Lys                                           | Cys                                                                   | Glu                                                          | Gln                                                          | His<br>45                                                  | Leu                                                | Gly                                                                           | His                                                                                    |                                                      | ,                          | ٠     |
| Asn                                                           | Ala<br>50                                                                    | Met                                                                | Tyr                                                                 | Trp                                                                 | Tyr        | <b>Lys</b><br>55                                                              | Gln                                                                  | Ser                                           | Ala                                                                   | ГÀЗ                                                          | <b>Lys</b><br>60                                             | Pro                                                        | Leu                                                | Glu                                                                           | Leu                                                                                    |                                                      |                            |       |
| Met<br>65                                                     | Phe                                                                          | Val                                                                | Tyr                                                                 | Ser                                                                 | Leu<br>70  | Glu                                                                           | Glu                                                                  | Arg                                           | <b>V</b> al                                                           | Glu<br>75                                                    | Asn                                                          | Asn                                                        | Ser                                                | Val                                                                           | Pro<br>80                                                                              |                                                      |                            |       |
| Ser                                                           | Arg                                                                          | Phe                                                                | Ser                                                                 | Pro<br>85                                                           | Glu        | СХ́а                                                                          | Pro                                                                  | Asn                                           | Ser<br>90                                                             | Ser                                                          | His                                                          | Leu                                                        | Phe                                                | Leu<br>95                                                                     | His                                                                                    |                                                      |                            |       |
| Leu                                                           | His                                                                          | Thr                                                                | Leu<br>100                                                          | Gln                                                                 | Pro        | Glu                                                                           | Asp                                                                  | Ser<br>105                                    | Ala                                                                   | Leu                                                          | Tyr                                                          | Leu                                                        | Cys<br>110                                         | Ala                                                                           | Ser                                                                                    | •                                                    | *                          |       |
| Ser                                                           | Gln                                                                          | Asp<br>115                                                         | Aŗg                                                                 | Thr                                                                 | Ser        | Ser                                                                           | Ser<br>120                                                           | Tyr                                           | Glu                                                                   | Gln                                                          | Tyr                                                          | Phe<br>125                                                 | 2.5                                                | Pro                                                                           | Gly                                                                                    | ; •                                                  | ÷                          | ٠.    |
| Thr                                                           | Arg<br>130                                                                   | Leu                                                                | Thr'                                                                | Val                                                                 | Thr        | G1u<br>135                                                                    | Asp                                                                  | Leu                                           | Lys                                                                   | Asn                                                          | Val<br>140                                                   | Phe                                                        | Pro                                                | Pro                                                                           | Glu                                                                                    | •••                                                  |                            | •     |
| Val<br>145                                                    | Ala                                                                          | Val                                                                | Phe                                                                 | G1u                                                                 | Pro<br>150 | Ser                                                                           | G1 u                                                                 | Ala                                           | Gľu                                                                   | 11e<br>155                                                   | Ser                                                          | His                                                        | Thr                                                | Gln                                                                           | Lys<br>160                                                                             | •                                                    | . •                        |       |
| Ala                                                           | Thr                                                                          | Leu                                                                | Val                                                                 | Cys<br>165                                                          | Leu        | Ala                                                                           | Thr                                                                  | Gly                                           | Phe<br>170                                                            | Tyr                                                          | Pro                                                          | Asp                                                        | His                                                | Val<br>175                                                                    | Glu 📑                                                                                  |                                                      |                            | ٠     |
| Leu                                                           | Ser                                                                          | Trp                                                                | Trp<br>180                                                          | Val                                                                 | Asn        | Gly                                                                           | Lys                                                                  | Glu<br>185                                    | Val                                                                   | His                                                          | Ser                                                          | Gly                                                        | Val<br>190                                         | Ser                                                                           | Thr                                                                                    | ·.<br>:                                              |                            |       |

|     |                         |                   |                          |                          |                         | . 1                     |                   |                          | 1                        | 4.               |                     |                   |                                        |                          |                         |                  |                      |                                               |
|-----|-------------------------|-------------------|--------------------------|--------------------------|-------------------------|-------------------------|-------------------|--------------------------|--------------------------|------------------|---------------------|-------------------|----------------------------------------|--------------------------|-------------------------|------------------|----------------------|-----------------------------------------------|
|     | Asp                     | Pro               | Gln                      | Pro                      | Len                     | Lvs                     | Glu               | Gln                      | Pro                      | Ala              | Leu                 | Asn               | Asp                                    | Ser                      | Arg                     | Tvr              |                      |                                               |
|     |                         |                   | 195                      |                          |                         | ,                       |                   | 200                      |                          | .):              |                     |                   | 205                                    |                          |                         |                  |                      | • •                                           |
|     |                         |                   |                          |                          |                         | 1 ;1                    |                   |                          |                          |                  |                     |                   |                                        |                          |                         |                  | 1                    |                                               |
|     | Cvs                     | Leu               | Ser                      | Ser                      | Arg                     | Leu                     | Arq               | Val                      | Ser                      | Ala              | Thr                 | Phe               | Trp                                    | Gln                      | Asn                     | Pro.             | i i sa               | · s .                                         |
| -   | -4-                     | 210               |                          |                          |                         |                         |                   |                          |                          |                  |                     |                   |                                        |                          |                         |                  | i i i i<br>g fjylugi | **                                            |
|     |                         |                   |                          |                          |                         |                         |                   |                          |                          |                  |                     |                   |                                        |                          |                         |                  |                      |                                               |
|     | Arq                     | Asn               | His                      | Phe                      | Arq                     | Cys                     |                   |                          |                          |                  |                     |                   |                                        |                          |                         | Asn              |                      |                                               |
|     | 225                     |                   |                          |                          |                         |                         |                   |                          |                          |                  |                     |                   |                                        |                          |                         |                  |                      |                                               |
|     |                         |                   |                          |                          |                         |                         |                   |                          | -                        |                  |                     | 13.75             | :<br>::::::::::::::::::::::::::::::::: | ur<br>Nasa               |                         |                  | i alia               |                                               |
|     | Asp                     | Glu               | Trp                      | Thr                      | Gln                     | Asp                     | Arg               | Ala                      | Lys                      | Pro              | Val                 | Thr               | Gln                                    | Ile                      | Val                     | Ser              |                      | r<br>Sisteman                                 |
|     | -                       |                   | -                        |                          | 245                     |                         |                   | ,                        |                          | 250              |                     |                   |                                        |                          | 255                     | , ,              |                      |                                               |
|     |                         |                   |                          |                          |                         | ۴.                      | :                 | r                        |                          |                  |                     |                   |                                        |                          |                         |                  | 1.35                 |                                               |
|     | Ala                     | Glu               | Ala                      | Trp                      | Gly                     | Arg                     | Ala               | Asp                      | Cys                      | Gly              | Phe                 | Thr               | Ser                                    | Glu                      | Ser                     | Tyr              |                      |                                               |
|     |                         | •                 |                          | 260                      | - 1                     | , -                     |                   |                          | 265                      |                  |                     |                   |                                        | 270                      |                         |                  |                      | 18 X 18 18 18 18 18 18 18 18 18 18 18 18 18   |
|     |                         |                   |                          |                          |                         | ,                       |                   |                          | ı                        |                  |                     |                   |                                        |                          | ai.                     | B + 1.1.         | . hb                 | 11.75                                         |
|     | Gln                     | Gln               | Gly                      | Val                      | Leu                     | Ser                     | Ala               | Thr                      | Ile                      | Leu              | Tyr                 | Glu               | Ile                                    | Leu                      | Leu                     | Gly              |                      |                                               |
|     |                         |                   | 275                      |                          |                         |                         |                   | 280                      |                          |                  |                     |                   | 285                                    |                          |                         |                  |                      | 4.440 5.5                                     |
|     |                         |                   |                          |                          |                         |                         | 1                 |                          |                          |                  |                     | ,                 |                                        |                          |                         |                  | is thus a            | 13 50                                         |
|     | Lys                     | Ala               | Thr                      | Leu                      | Tyr                     | Ala                     |                   | Leu                      | Val                      | Ser              | Ala                 |                   |                                        |                          |                         |                  | ( .                  | $ \sigma  = \int_{X_{n+1}}^{T_{n+1}} f(x) dx$ |
|     |                         | 290               |                          | ķ                        |                         |                         | 295               |                          |                          |                  |                     | 300               |                                        |                          | . ( <u>1</u> ) - 1      |                  | er mælli             | 1.                                            |
|     |                         |                   |                          |                          |                         |                         |                   |                          |                          |                  |                     |                   |                                        |                          |                         |                  |                      |                                               |
|     |                         |                   |                          |                          |                         | Asp                     |                   |                          |                          |                  |                     |                   |                                        |                          |                         |                  |                      | •                                             |
|     | 305                     |                   |                          | 7 1                      |                         | '310                    | 83.3              |                          |                          | V                | ٠. ٩                | ٠.                |                                        | ,1 ± 5                   | , .                     | 3                |                      |                                               |
|     | ,                       |                   |                          |                          | £1                      |                         |                   |                          |                          | 7:               |                     |                   |                                        |                          |                         |                  |                      |                                               |
|     |                         |                   |                          |                          |                         |                         |                   |                          |                          |                  |                     |                   |                                        |                          |                         |                  |                      |                                               |
|     |                         | )> 70             |                          |                          | •                       | ٠,                      | ~ PH              | 0.20                     | . 7. 5                   | 4.0              |                     | 1.1               |                                        | 15)                      |                         |                  |                      | •                                             |
|     |                         | 1> 2              |                          |                          |                         |                         | ,                 |                          |                          |                  | •                   |                   |                                        |                          |                         |                  |                      |                                               |
|     |                         | 2> PI             |                          |                          |                         |                         |                   |                          |                          |                  |                     |                   |                                        | _                        |                         |                  | •                    |                                               |
|     | <21.                    | 3> H              | omo s                    | sapı                     | ens                     |                         |                   |                          | <i>:</i> .               |                  |                     |                   | ** *                                   | :M:                      | ક પ્રા                  | មេនធំ            |                      | 9 4                                           |
|     | -401                    | 1 7               | co                       |                          |                         |                         |                   |                          |                          |                  |                     |                   |                                        |                          |                         |                  |                      |                                               |
|     |                         | 0> 76             |                          | Con                      | 8                       | T 011                   | Lou               | Tara                     | 17-1                     | Wa 1             | Ţhr                 | λ1 =              | Cor                                    | T.O.                     | than .                  | T.O11            |                      |                                               |
|     | met                     | Ser               | теп                      | Ser                      | 5                       | nen                     | nea               |                          | AGT                      | 10               | im                  | ALG               | 261                                    | neu                      | 15                      | nea              |                      |                                               |
|     |                         |                   |                          |                          | J                       |                         |                   | ٠.                       |                          | 10               |                     |                   |                                        |                          | 13                      |                  |                      |                                               |
|     | Glv                     | Pro               | Glv                      | Tle                      | Δla                     | Gln                     | Lvs               | Tle                      | Thr                      | Gln              | Thr                 | Gln               | Pro                                    | Glv                      | Met                     | Phe              |                      |                                               |
|     | OLY                     | LLO               | GTA                      | 20                       | ru,a                    | O,ZII                   | <b></b> y 0       |                          | 25                       | <b>J</b>         |                     | 03.41             | 2 4,0                                  | 30                       | 220,0                   |                  |                      | ,                                             |
|     |                         |                   |                          | 20                       |                         |                         |                   |                          |                          |                  |                     |                   |                                        | (00                      |                         |                  |                      |                                               |
|     | Val                     | Gln               | Glu                      | Lvs                      | Glu                     | Ala                     | Val               | Thr                      | Leu                      | Asp              | Суз                 | Thr               | Tvr.                                   | Asp                      | Thr                     | Ser              |                      | •                                             |
|     |                         | 02.               | 35                       | -1-                      |                         |                         |                   | 40                       |                          |                  | -1-                 |                   | 45                                     | <u>F</u> -               |                         |                  |                      |                                               |
|     |                         |                   | •                        |                          |                         |                         | :                 |                          |                          | •                |                     |                   |                                        |                          |                         |                  |                      |                                               |
|     | Asp                     | Gln               | Ser                      | Tvr                      | Glv                     | Leu                     | Phe               | Trp                      | Tyr                      | Lys              | Gln                 | Pro               | Ser                                    | Ser                      | Gly                     | Glu              |                      |                                               |
|     |                         | 50                |                          | -20                      | 2                       | - : .                   | 55                | <i>3=</i> ( <b>€</b> 0   | - <b>.</b>               |                  | - ,                 | 60                |                                        |                          | •                       | . 1              | •                    | . '                                           |
|     |                         |                   |                          |                          |                         |                         |                   |                          |                          |                  | •                   |                   |                                        |                          |                         |                  |                      |                                               |
|     |                         |                   |                          |                          |                         |                         |                   |                          |                          |                  |                     |                   |                                        |                          |                         |                  |                      |                                               |
|     | Met                     | Ile               | Phe                      | Leu                      | Ile                     | Tyr                     | Gln               | Gly:                     | Ser                      | Tyr              | Asp                 | Glu               | Gln                                    | Asn                      | Ala                     | Thr              |                      |                                               |
|     | Met<br>65               | Ile               | Phe                      | Leu                      | Ile                     | Tyr<br>70               | Gln               | Gly                      | Ser                      | Tyr              | Asp<br>75           | Glu               | GĻn                                    | Asn                      | Ala                     | Thr.<br>80       |                      |                                               |
|     |                         | Ile               | Phe                      | Leu                      | Ile                     | Tyr<br>70               |                   | Gly                      | Ser                      | Tyr              | Asp<br>75           | Glu               | GĻn                                    | Asn                      | Ala                     |                  |                      |                                               |
|     | 65                      |                   |                          |                          |                         | 70                      | 7.5               |                          |                          |                  | 75                  |                   |                                        |                          |                         | 80               |                      |                                               |
|     | 65                      |                   |                          |                          |                         | 70                      | 7.5               | Phe                      |                          |                  | Asp<br>75<br>Ala    |                   | Lys;                                   |                          |                         | 80               |                      |                                               |
| . • | 65                      |                   |                          |                          | Şer                     | 70                      | 7.5               |                          |                          | Lys              | 75                  |                   |                                        |                          | Ala                     | 80               |                      |                                               |
|     | 65<br>Glu               | Gly               | Arg                      | Tyr                      | Şer<br>85               | 70<br>Ley               | Asn               | Phe                      | Gln                      | Lys<br>90        | 75                  | Arg               | <b>Lyş</b> )                           | Ser                      | Ala<br>95               | 80<br>Asn        |                      |                                               |
| •   | 65<br>Glu               | Gly               | Arg                      | Tyr                      | Şer<br>85               | 70<br>Ley               | Asn               | Phe                      | Gln                      | Lys<br>90        | 75<br>Ala           | Arg               | <b>Lyş</b> )                           | Ser                      | Ala<br>95               | 80<br>Asn        | 5 :                  |                                               |
| •   | 65<br>Glu               | Gly               | Arg                      | Tyr<br>Ser               | Şer<br>85               | 70<br>Ley               | Asn               | Phe                      | Gln<br>Gly               | Lys<br>90        | 75<br>Ala           | Arg               | <b>Lyş</b> )                           | Ser                      | Ala<br>95               | 80<br>Asn        | 5 *                  |                                               |
|     | 65<br>Glu<br>Leu        | Gly<br>Val        | Arg<br>Ile               | Tyr<br>Ser<br>100        | Şer<br>85<br>Ala        | 70<br>Ley<br>Ser        | Asn<br>Gln        | Phe                      | Gln<br>Gly<br>105        | Lys<br>90<br>Asp | 75<br>Ala<br>Ser    | Arg<br>Ala        | Lys<br>Met                             | Ser<br>Tyr<br>110        | Ala<br>95<br>Phe        | 80<br>Asn<br>Cys | 5 •                  |                                               |
| •   | 65<br>Glu<br>Leu        | Gly<br>Val        | Arg<br>Ile               | Tyr<br>Ser<br>100        | şer<br>85<br>Ala        | 70<br>Ley<br>Ser        | Asn<br>Gln        | Phe                      | Gln<br>Gly<br>105        | Lys<br>90<br>Asp | 75<br>Ala           | Arg<br>Ala        | Lys<br>Met                             | Ser<br>Tyr<br>110        | Ala<br>95<br>Phe        | 80<br>Asn<br>Cys |                      |                                               |
| •   | 65<br>Glu<br>Leu        | Gly<br>Val        | Arg<br>Ile<br>Arg        | Tyr<br>Ser<br>100        | Şer<br>85<br>Ala        | 70<br>Ley<br>Ser        | Asn<br>Gln        | Phe<br>Leu<br>Gly        | Gln<br>Gly<br>105        | Lys<br>90<br>Asp | 75<br>Ala<br>Ser    | Arg<br>Ala        | Lys<br>Met                             | Ser<br>Tyr<br>110        | Ala<br>95<br>Phe        | 80<br>Asn<br>Cys |                      |                                               |
|     | 65<br>Glu<br>Leu<br>Ala | Gly<br>Val<br>Met | Arg<br>Ile<br>Arg<br>115 | Tyr<br>Ser<br>100<br>Glu | Ser<br>85<br>Ala<br>Gly | 70<br>Ley<br>Ser<br>Ala | Asn<br>Gln<br>Gly | Phe<br>Leu<br>Gly<br>120 | Gln<br>Gly<br>105<br>Gly | Lys<br>90<br>Asp | 75<br>Ala<br>Ser    | Arg<br>Ala<br>Leu | Lys<br>Met<br>Thm<br>125               | Ser<br>Tyr<br>110<br>Phe | Ala<br>95<br>Phe<br>Gly | 80 Asn Cys,      |                      |                                               |
| •   | 65<br>Glu<br>Leu<br>Ala | Gly<br>Val<br>Met | Arg<br>Ile<br>Arg<br>115 | Tyr<br>Ser<br>100<br>Glu | Ser<br>85<br>Ala<br>Gly | 70<br>Ley<br>Ser<br>Ala | Asn<br>Gln<br>Gly | Phe<br>Leu<br>Gly<br>120 | Gln<br>Gly<br>105<br>Gly | Lys<br>90<br>Asp | 75 Ala Ser Lys, Gln | Arg<br>Ala<br>Leu | Lys<br>Met<br>Thm<br>125               | Ser<br>Tyr<br>110<br>Phe | Ala<br>95<br>Phe        | 80 Asn Cys,      |                      |                                               |

| Val Tyr Gln Leu Arg Asp Ser Lys Ser Ser Asp Lys Ser Val                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                         |
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| Phe Thr Asp Phe Asp Ser Gln Thr Asn Val Ser Gln Ser Lys                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Asp Ser                                                                                                                                                                 |
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| Pro Ser Pro Glu Ser Ser Cvs Asp Val Lys Leu Val Glu Lys                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Ser Phe                                                                                                                                                                 |
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| Glu Thr Asp Thr Asn Leu Asn Phe Gln Asn Leu Ser Val Ile                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                         |
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| 260 265 270                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | The state of the stay term of                                                                                                                                           |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | edije, av dyška kasti                                                                                                                                                   |
| Arg Leu Trp Ser Ser                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | With a mass of the constraint                                                                                                                                           |
| 275                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                         |
| and the control of th |                                                                                                                                                                         |
| All the planting designs and the second of t |                                                                                                                                                                         |
| <210> 764                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                         |
| ZTIN 1000                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                         |
| <212> DNA<br><213> Homo sapiens                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                         |
| <213> Homo sapiens                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                         |
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80
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| Leu        | Ile        | Ile        | Thr        | Thr<br>85 | Ļ <b>ys</b> | Lys        | Arg        | Glu        | Ala<br>90 | Arg        | Gln | Ile        | Leu        | Asp<br>95 | Gln        |   |
|------------|------------|------------|------------|-----------|-------------|------------|------------|------------|-----------|------------|-----|------------|------------|-----------|------------|---|
| Thr        | Pro        | Val        | Lys<br>100 | Glu       | Leu         | Val        | Ser        | Leu<br>105 | Lys       | Trp        | Lys | Arg        | Tyr<br>110 | Gly       | Arg        |   |
| Pro        | Tyr        | Phe<br>115 | Cys        | Met       | Leu         | Gly        | Ala<br>120 | Ile        | Tyr       | Leu        | Leu | Tyr<br>125 | Ile        | Ile       | Cys        |   |
| Phe        | Thr<br>130 | Met        | Cys        | Cys       | Ile         | Tyr<br>135 | Arg        | Pro        | Leu       | ry.        | 140 | Arg        | Thr        | Asn       | Asn        |   |
| Arg<br>145 | Thr        | Ser        | Pro        | Arg       | Asp<br>150  | Asn        | Thr        | Leu        | Leu       | Gln<br>155 | Gln | Lys        | Leu        | Leu       | Gln<br>160 |   |
|            |            |            | , i ,      | 165       | •           | ; ··       | į į, š     | ٠,         | 170       | 11         |     | . *        |            | 175       | '          |   |
|            |            |            | 180        | : .**     | Ala         | ., .       |            | 185        |           |            |     | Sept.      | 190        |           |            |   |
|            |            | 195        |            |           | Val         |            | 200        |            |           |            |     | 205        | 2          |           |            |   |
| •          | 210        |            |            |           | Leu         | 215        |            |            | •         |            | 220 |            |            |           |            |   |
| 225        |            |            |            |           | Leu<br>230  |            |            |            |           | 235        |     |            |            |           | 240        |   |
|            |            |            |            | 245       |             |            |            |            | 250       |            |     |            |            | 255       | Arg.       |   |
| _          |            |            | 260        |           | Gly         | :          |            | 265        |           |            |     |            | 270        | )         |            |   |
|            | •          | 275        |            |           |             | ,          | 280        |            |           |            |     | 285        |            |           | Leu        |   |
| •          | 290        |            |            |           |             | 295        |            |            |           |            | 300 | ĺ          |            |           | Glu        |   |
| 305        |            |            | ,          |           | 310         |            |            |            |           | 315        |     |            |            |           | Phe<br>320 |   |
|            |            |            |            | 325       | •           |            |            |            | 330       | )          |     |            |            | 335       |            |   |
|            |            |            | 340        | )         |             |            |            | 345        | i         |            | ,   |            | . 350      | ,         | Ala        |   |
|            |            | 355        | 5          |           |             |            | 360        | )          |           |            |     | 365        | 5          | ,         | His        |   |
| Trp        | 370        |            | Ala        | His       | s Glu       | 375        |            | Glu        | ı Lev     | Trp        | 380 | Ala        | a Glr      | n Ile     | vál        |   |
| Ala        | Thr        | Thi        | val        | L Met     | Leu         | Glu        | a Arç      | J Lys      | Let       | ı Pro      | Arc | g Cy:      | s Le       | ı Tr      | Pro        | , |

| 385                                                  |                                  |                                |                         | •                                                 |                        |                                |                            |                                              |                           |                                |                                |                                |                                       |                            |                                |     |     |    |
|------------------------------------------------------|----------------------------------|--------------------------------|-------------------------|---------------------------------------------------|------------------------|--------------------------------|----------------------------|----------------------------------------------|---------------------------|--------------------------------|--------------------------------|--------------------------------|---------------------------------------|----------------------------|--------------------------------|-----|-----|----|
|                                                      |                                  |                                |                         |                                                   | 390                    |                                | ٠                          | • • ;                                        | 1 2 - , 1                 | 395                            |                                |                                | •                                     |                            | 400                            |     |     |    |
| Arg                                                  | Ser                              | Gly                            | Ile                     | Cys<br>405                                        |                        | Arg                            |                            |                                              | Gly<br>410                |                                |                                |                                | Arg                                   | Trp<br>415                 | Phe                            |     |     |    |
| Leu                                                  | Arg                              | Val                            | Glu<br>420              | Asp                                               | Arg                    | Gln                            | _                          |                                              | Asn                       | _                              |                                | _                              |                                       | Gln                        | Arg                            |     |     |    |
| Tyr                                                  | Ala                              | Gln<br>435                     |                         |                                                   |                        |                                | -                          |                                              | Ser                       |                                |                                |                                | _                                     | Lys                        | Asp                            | - : | . ( |    |
| Ser                                                  | Val<br>450                       | Glu                            |                         |                                                   |                        |                                |                            |                                              | Pro                       |                                |                                |                                |                                       |                            | Ser                            |     | •   |    |
| Leu<br>465                                           | Pre                              | Met                            |                         |                                                   |                        |                                |                            |                                              | Thr                       |                                |                                |                                |                                       |                            |                                |     |     |    |
| Trp                                                  | Glu                              | Arg                            | Leu                     | Arg<br>485                                        |                        | _                              |                            |                                              | Arg<br>490                |                                |                                |                                |                                       |                            |                                | ,   |     |    |
| Ile                                                  | Asn                              | Arg                            | Gly<br>500              | Leu                                               | G1u                    | Asp                            | Gly                        | Glu<br>505                                   | Ser                       | Trp                            |                                | Tyr                            | Gln<br>510,                           |                            |                                |     |     |    |
| <210<br><211<br><212                                 | > 13                             | 34                             | ्री करा                 | មេជា                                              | :<br>_ #**             | .'.e                           | 7.<br>23° s                |                                              |                           |                                | 990<br>977                     |                                |                                       |                            |                                | , · |     |    |
|                                                      |                                  |                                |                         |                                                   |                        |                                |                            |                                              |                           |                                |                                |                                |                                       |                            |                                |     |     |    |
| <213                                                 | / nc                             | omo :                          | sapı                    | ens                                               |                        |                                | 3.3                        |                                              |                           |                                | يخ د                           | w.r.t                          |                                       | 2°, 3                      |                                |     | •   | ٠. |
| <400                                                 | > 76                             | 67                             | FR. 3                   |                                                   | Ĺeu                    | Ser                            |                            | Asp                                          | Arg<br>10                 | His                            |                                |                                | ŋξ:                                   | Leu<br>15                  | Gln                            |     | ٠   |    |
| <400<br>Met                                          | )> 76<br>Tyr                     | 67<br>Asn                      | Leu                     | Leu<br>,5                                         |                        | Asn                            | Tyr                        |                                              |                           | - \                            | Gly                            | Asp                            | ηξ:<br>H <b>i</b> s                   | 15                         |                                |     | ٠   |    |
| <400<br>Met<br>Pro                                   | )> 76<br>Tyr<br>Leu              | 67<br>Asn<br>Asp               | Leu<br>Leu<br>20        | Leu<br>5<br>Val                                   | Pro                    | Asn                            | Tyr                        | Gln<br>25                                    | 10                        | Leu                            | Gly<br>Thr                     | Asp<br>Pro                     | His<br>Phe<br>30                      | 15<br>Lys                  | Leu                            |     | ·   |    |
| <400<br>Met<br>Pro                                   | > 76<br>Tyr<br>Leu<br>Gly        | Asn Asp Val 35                 | Leu<br>Leu<br>20<br>Glu | Leu<br>5<br>Val<br>Gly                            | Pro<br>Asn             | Asn                            | Tyr<br>His<br>Val          | Gln<br>25<br>Met                             | Gly                       | Leu                            | Gly<br>Thr<br>His              | Asp<br>Pro<br>Leu<br>45        | His<br>Phe<br>30<br>Met               | 15<br>Lys<br>Gln           | Leu<br>Lys                     |     |     |    |
| <400<br>Met<br>Pro<br>Ala                            | Tyr Leu Gly Lys 50               | Asn Asp Val 35                 | Leu<br>Leu<br>20<br>Glu | Leu 5<br>Val Gly                                  | Pro Asn Trp            | Asn<br>Thr<br>Thr<br>55        | Tyr His Val 40             | Gln<br>25<br>Met<br>Gly                      | 10<br>Gly<br>Phe          | Leu<br>Gln<br>Leu              | Gly<br>Thr<br>His<br>Thr       | Asp<br>Pro<br>Leu<br>45<br>Ser | Phe 30 Met                            | 15<br>Lys<br>Gln<br>Leu    | Leu<br>Lys<br>Tyr              |     |     |    |
| <400<br>Met<br>Pro<br>Ala<br>Arg<br>Asp<br>65        | From Tyr  Leu  Gly  Lys  50  Leu | Asp Val 35 His                 | Leu<br>20<br>Glu<br>Thr | Leu<br>5<br>Val<br>Gly<br>Gln                     | Pro Asn Trp Asp 70     | Asn<br>Thr<br>Thr<br>55<br>Ser | Tyr His Val 40 Tyr         | Gln<br>25<br>Met<br>Gly                      | 10<br>Gly<br>Phe<br>Pro   | Leu<br>Gln<br>Leu<br>Glu<br>75 | Gly<br>Thr<br>His<br>Thr<br>60 | Asp<br>Pro<br>Leu<br>45<br>Ser | ne: His Phe 30 Met Thr                | Lys Gln Leu Leu            | Leu<br>Lys<br>Tyr<br>Glu<br>80 |     |     |    |
| <400<br>Met<br>Pro<br>Ala<br>Arg<br>Asp<br>65<br>Leu | Leu<br>Gly<br>Lys<br>50<br>Leu   | Asp<br>Val<br>35<br>His<br>Thr | Leu<br>20<br>Glu<br>Thr | Leu<br>5<br>Val<br>Gly<br>Gln<br>Ile<br>Thr<br>85 | Pro Asn Trp 70 Lys     | Asn Thr 55 Ser                 | Tyr His Val 40 Tyr Ser     | Gln<br>25<br>Met<br>Gly<br>Gly               | 10 Gly Phe Pro Asp Ala 90 | Leu<br>Gln<br>Leu<br>Glu<br>75 | Gly Thr His Gln Gln            | Asp Pro Leu 45 Ser Ser         | His<br>Phe<br>30<br>Met<br>Thr<br>Leu | Lys Gln Leu Leu Asp 95     | Leu<br>Lys<br>Tyr<br>Glu<br>80 | •   |     |    |
| <400<br>Met  Pro  Ala  Arg  Asp 65  Leu  Thr         | Leu Gly Lys 50 Leu Ile           | Asp Val 35 His Thr             | Leu 20 Glu Thr Lys 100  | Leu<br>5<br>Val<br>Gly<br>Gln<br>Thr<br>85<br>Glu | Pro Asn Trp Asp 70 Lys | Asn Thr 55 Ser Lys Val         | Tyr His Val 40 Tyr Ser Arg | Gln<br>25<br>Met<br>Gly<br>Gly<br>Leu<br>105 | 10 Gly Phe Pro Asp Ala 90 | Leu Glu 75 Arg                 | Gly Thr His 60 Gln Gln         | Asp Pro Leu 45 Ser Ser Ile Arg | Phe 30 Met Thr Leu Leu Tyr 110        | Lys Gln Leu Leu Asp 95 Gly | Leu Lys Tyr Glu 80 Gln Arg     | •   |     |    |

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Asp Asn Thr Leu Leu
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Pro Lys Asp Asp Ile
35

Ala Ile Ile Ile Leu
50

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Pro Lys Asp Asp Ile Arg Leu Val Gly Glu Leu Val Thr Val Ile Gly
35 40 45

Ala Ile Ile Ile Leu Leu Val

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Met Val Leu Val Thr Met Val 35

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Leu Val Leu

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1.

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25 '

30

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Tyr Ile Ile Phe 50

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Ala Asn Tyr Asn Val Asp Leu Pro Phe Met Tyr Ser Ile Thr Tyr Ala 35 40 45

Ala Phe Ala Ile Ile Ala Thr Leu Leu Met Leu Asn Leu Leu Ile Ala 50

Met Met Gly Asp Thr His Trp Arg Val Ala His Glu Arg Asp Glu Leu 65 70 75 2 299 cre 710 80

Trp Arg Ala Gln Ile Val Ala Thr Thr Val Met Leu Glu Arg Lys Leu
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Pro Arg Cys Leu Trp Pro Arg Ser Gly Ile Cys Gly Arg Glu Tyr Gly 100 105 110

Leu Gly Asp Arg Trp Phe Leu Arg Val Glu Asp Arg Gln Asp Leu Asn 115 120 125

Arg Gln Arg Ile Gln Arg Tyr Ala Gln Ala Phe His Thr Arg Gly Ser 130 135 140

Glu Asp Leu Asp Lys Asp Ser Val Glu Lys Leu Glu Leu Gly Cys Pro 145 150 155 160

ST 7 15

Phe Ser Pro His Leu Ser Leu Pro Met Pro Ser Val Ser Arg Ser Thr

Ser Arg Ser Ser Ala Asn Trp Glu Arg Leu Arg Gln Gly Thr Leu Arg 180 185 190

Arg Asp Leu Arg Gly Ile Ile Asn Arg Gly Leu Glu Asp Gly Glu Ser 195 200 205

Trp Glu Tyr Gln Ile 210

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the grant and the Fig. Chr. First

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                           ្នាក្នុង ខេត្តប្រើប្រើការបើក បើកកាត់កាត់ត្រូវតែការពីការបេរីសេវត្ថា ប្រមុវត្ថិទីវេវាជម្រូវត្រៅបានប្រើប្រឹ
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|--------------|--------------|--------------|------------|------------|------------|--------------|------------|------------|------------|------------|------------|---------------|---------------|-------------|------------------|------------|
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|              | > PR         |              | apie       | ns         | ŧ          | ,            |            | •          |            |            |            |               | •             |             | i.               |            |
| <400         | > 77         | 7            |            |            |            |              | , -<br>_   | 1. ·       | <b>.</b> . |            | 77-        | mb            | <b>M</b>      | nh a        | T1.              |            |
|              |              |              | į          | 5          | ,          |              |            |            | 10         | •          |            |               |               | Phe<br>15   |                  |            |
| Leu          | Ile          | Gly          | Leu<br>20  | Pro        | Gly        | Leu          | Glů        | Glu<br>25  | Ala        | Gln        | Phe        | Trp           | Jeu<br>30     | Ala         | Phe              |            |
| Pro          | Leu          | Cys<br>35    | Ser        | Leu        | Tyr        | Leu          | Ile<br>40  | Ala        | Val        | Leu        | Gly        | Asn<br>45     | Leu           | Thr         | Ile              |            |
| Ile          | Tyr<br>50    | Ile          | Val        | Arg        | Thr        | Glu<br>55    | His        | Ser        | Leu        | His        | Glu<br>60  | Pro           | Met           | Tyr         | Ilē              |            |
| Phe<br>65    | Leu          | Cys          | Met        | Leu        | Ser<br>70  | Gly          | Ile        | Asp        | Ile        | Leu<br>75  | Ile        | Ser           | Thr           | Ser         | Ser<br>80        | •          |
| Met          | Pro          | ГЛЗ          | Met        | Leu<br>85  | Ala        | Ile          | Phe        | Trp        | Phe<br>90  | Asn        | Ser        | Thr           | Thr           | Ile<br>95   | Gln              |            |
| Phe          | Asp          | Ala          | Cys<br>100 | Leu        | Leu        | Gln          | Met        | Phe<br>105 | Ala        | Ile        | His        | Ser           | Leu<br>110    | Ser         | Gly              |            |
| Met          | Glu          | Ser<br>115   | Thr        | Val        | Leu        | Leu          | Ala<br>120 | Met        | Ala        | Phe        | Asp        | Arg<br>125    | Tyr           | Val         | Ala <sub>.</sub> |            |
| Ile          | Cys<br>130   | His          | Pro        | Leu        | Arg        | His<br>135   | Ala        | Thr        | Val        | Leu        | Thr<br>140 | Leu           | Pro           | Arg         | Val              | •          |
| Thr<br>145   | Lys          | Ile          | Gly        | Val        | Ala<br>150 |              | Val        | Val        | Arg        | Gly<br>155 | Ala        | Ala           | Leu           | Met         | Ala<br>160       | 7 T        |
| Pro          | Leu          | Pro          | Val        | Phe<br>165 | Ile        | ГÀЗ          | Gln        | Leu        | Pro<br>170 | Phe        | Cys        | Arg           | Ser           | Asn<br>175  | Ile              |            |
| Leu          | Ser          | His          | Ser<br>180 | Tyr        | Суз        | Leu          | His        | Gln<br>185 |            | Val        | Met        | Lys           | Leu<br>190    | Ala         | Cys              |            |
| Asp          | Asp          | Ile<br>195   | Arg        | Val        | Asn        | Val          | Val<br>200 |            | Gly        | Leu        | Ile        | Val<br>205    | Ile           | Ile         | Ser              |            |
|              |              |              |            |            |            |              |            |            |            |            |            |               |               |             |                  | ×4         |

Ala Ile Gly Leu Asp Ser Leu Leu Ile Ser Phe Ser Tyr Leu Leu Ile

Leu Lys Thr Val Leu Gly Leu Thr Arg Glu Ala Gln Ala Lys Ala Phe

Gly Thr Cys Val Ser His Val Cys Ala Val Phe Ile Phe Tyr Val Pro

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Phe Ilc Gly Leu Ser Met Val His Arg Phe Ser Lys Arg Arg Asp Ser
                                                       260 265
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  Pro Leu Pro Val Ile Leu Ala Asn Ile Tyr Leu Leu Val Pro Pro Val
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Thr His Ala Ser Glu Pro

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ကြ<del>င့် ကြသာသို့</del> တွင် သို့သောကျသည်။ အသော အသောကျသည် အသောကြသည်မှု သည်သို့တာ မြန်မာသည်။ အသည်
ကြန်မာ့ အမြည့်မို့များသူတွင် စားသည် အသိသည် သောလိုကြသည် အသည် အသည်သို့တွင် ကြာသည်။ အ
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          210 215 Transport and the 215 to the transport of the 225 to the transport of the 215 to the 215 to the transport of the 215 to the transport of the 215 to the 2
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225 230 235 240
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Cys Ile Ala Cys Gly Val Asn Leu Asn Ser Ser Arg Gln Ser Arg Ile
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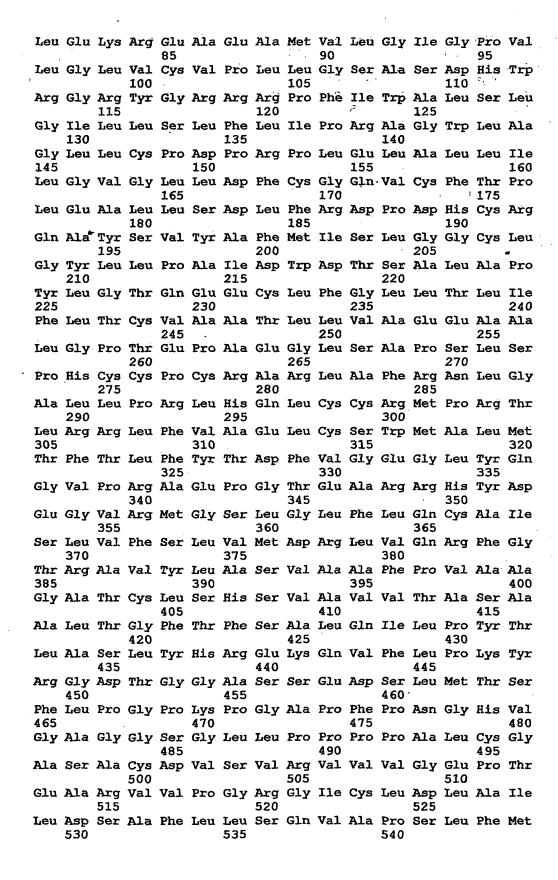
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